Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

PART TWO

Systemic Approach to Differential Diagnosis

SECTION I

Cardiopulmonary Disorders

Arrhythmias

Differential Diagnosis

Slow, Irregular Rhythms
- Sinus bradyarrhythmias
- Sinus arrest
- Sick sinus syndrome
- High-grade second-degree atrioventricular (AV) block

Slow, Regular Rhythms
- Sinus bradycardia
- Complete AV block with ventricular escape rhythm
- Atrial standstill with ventricular escape rhythm

Fast, Irregular Rhythms
- Atrial or supraventricular premature contractions
- Paroxysmal atrial or supraventricular tachycardia
- Atrial flutter

Atrial fibrillation
Ventricular premature contractions
Paroxysmal ventricular tachycardia

Fast, Regular Rhythms
Sinus tachycardia
Sustained supraventricular tachycardia
Sustained ventricular tachycardia

Normal, Irregular Rhythms (require no treatment)
Respiratory sinus arrhythmia
Wandering pacemaker

Arterial Thromboembolism

Clinical Findings

Acute Limb Paresis
Posterior paresis ("saddle" thrombus: most common presentation)
Monoparesis (right subclavian artery thrombus; second most common presentation in cats)
Intermittent claudication
Severe limb pain
Cool distal limbs
Cyanotic nail beds
Arterial pulse absent
Contracture of affected muscles
Vocalization (pain, distress)

Renal Infarction
Renal pain
Acute renal failure

Splenic Infarction
Lethargy
Anorexia
Vomiting
Diarrhea

Mesenteric Infarction
Abdominal pain
Vomiting
Diarrhea

Cerebral Infarction
Neurologic deficits
Seizures
Sudden death

Signs of Heart Failure
- Systolic murmur
- Gallop rhythm
- Tachypnea/dyspnea
- Weakness/lethargy
- Anorexia
- Arrhythmias
- Hypothermia
- Cardiomegaly
- Effusions
- Pulmonary edema

Hematologic and Biochemical Abnormalities
- Azotemia
- Increased alanine aminotransferase activity
- Increased aspartate aminotransferase activity
- Increased lactate dehydrogenase activity
- Increased creatine kinase activity
- Hyperglycemia
- Lymphopenia
- Disseminated intravascular coagulation

Aspiration Pneumonia

Etiology of Aspiration Pneumonia

Esophageal Disorders
- Megaesophagus
- Reflux esophagitis
- Esophageal obstruction
- Myasthenia gravis (localized)
- Bronchoesophageal fistulae

Localized Oropharyngeal Disorders
- Cleft palate
- Cricopharyngeal motor dysfunction
- Laryngoplasty
- Brachycephalic airway syndrome

Systemic Neuromuscular Disorders
- Myasthenia gravis
- Polyneuropathy
- Polymyopathy

Decreased Mentation
- General anesthesia
- Sedation
- Post ictus

Head trauma
Severe metabolic disease

Iatrogenic
Force-feeding
Stomach tubes

Vomiting (in combination with other predisposing factors)

Atrioventricular Valve Disease, Chronic (Mitral or Tricuspid Valve)

Potential Complications

Acute Worsening of Pulmonary Edema
Arrhythmias
- Frequent atrial premature contractions
- Paroxysmal atrial/supraventricular contractions
- Atrial fibrillation
- Ventricular tachyarrhythmias

Ruptured chordae tendineae
Iatrogenic volume overload
- Excessive fluid or blood administration
- High-sodium fluids

High sodium intake
Increased cardiac workload
- Physical exertion
- Anemia
- Infection/sepsis
- Hypertension
- Disease of other organ systems (pulmonary, hepatic, renal, endocrine)
- Environmental stress (heat, humidity, cold, etc.)

Inadequate medication for stage of disease
Erratic or improper drug administration
Myocardial degeneration and poor contractility

Causes of Reduced Cardiac Output
Arrhythmias
Ruptured chordae tendineae
Cough-related syncope
Left atrial tear, intrapericardial bleeding, cardiac tamponade
Secondary right-sided heart failure
Myocardial degeneration, poor contractility

Cardiomegaly

Differential Diagnosis

Generalized Cardiomegaly
- Dilated cardiomyopathy
- Pericardial effusion
- Mitral and tricuspid valve insufficiency
- Tricuspid dysplasia
- Pericardioperitoneal diaphragmatic hernia
- Ventricular septal defect
- Patent ductus arteriosus

Left Atrial Enlargement
- Mitral valve insufficiency
- Hypertrophic cardiomyopathy
- Early dilated cardiomyopathy (especially in Doberman Pinschers)
- Subaortic or aortic stenosis

Left Atrial and Ventricular Enlargement
- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy
- Mitral valve insufficiency
- Aortic valve insufficiency
- Ventricular septal defect
- Patent ductus arteriosus
- Subaortic or aortic stenosis
- Systemic hypertension
- Hyperthyroidism

Right Atrial and Ventricular Enlargement
- Advanced heartworm disease
- Chronic severe pulmonary disease
- Tricuspid valve insufficiency
- Atrial septal defect
- Pulmonic stenosis
- Tetralogy of Fallot
- Reversed-shunting congenital defects
- Pulmonary hypertension
- Mass lesion within right heart

Chylothorax

Diagnostic Criteria

Protein concentration is greater than 2.5 g/dL
Nucleated cell count ranges from 400 to 10,000/μL

Predominant cell type on cytology is the small lymphocyte (also see neutrophils, macrophages, plasma cells, and mesothelial cells)
Triglyceride concentration of pleural fluid is greater than that of serum (definitive test)

Causes of Chylothorax

Traumatic
- Blunt force trauma (e.g., vehicular trauma)
- Postthoracotomy

Nontraumatic
- Neoplasia (especially mediastinal lymphoma in cats)
- Cardiomyopathy
- Dirofilariasis
- Pericardial disease
- Other causes of right heart failure
- Lung lobe torsion
- Diaphragmatic hernia
- Systemic lymphangiectasia

Idiopathic (most commonly diagnosed)

Diagnostic Tests to Identify Underlying Cause of Chylothorax in Dogs and Cats

CBC, Serum Chemistry, Urinalysis
- Evaluation of systemic status

Cytologic Examination of Pleural Fluid
- Infectious agents
- Neoplastic cells

Thoracic Radiographs (after fluid removal)
- Cranial mediastinal masses
- Other neoplasia
- Cardiac disease
- Heartworm disease
- Pericardial disease

Ultrasonography (before fluid removal)
- Cranial mediastinum (masses)
- Echocardiography (cardiomyopathy, heartworm disease, pericardial disease, congenital heart disease)
- Ultrasound of body wall and pleural space (neoplasia, lung lobe torsion)

Heartworm Antibody and Antigen Tests
- Heartworm disease

Lymphangiography

- Preoperative and postoperative assessment of thoracic duct

Congenital Heart Disease

Breed Predispositions

Patent Ductus Arteriosus
Maltese, Pomeranian, Shetland Sheepdog, English Cocker Spaniel, English Springer Spaniel, Keeshond, Bichon Frise, toy and miniature Poodle, Yorkshire Terrier, Collie, Cocker Spaniel, German Shepherd, Chihuahua, Kerry Blue Terrier, Labrador Retriever, Newfoundland; female affected more than male

Subaortic Stenosis
Newfoundland, Golden Retriever, Rottweiler, Boxer, German Shepherd, English Bulldog, Great Dane, German Shorthaired Pointer, Bouvier des Flandres, Samoyed

Aortic Stenosis
Bull Terrier

Pulmonic Stenosis
English Bulldog (male affected more than female), Mastiff, Samoyed, Miniature Schnauzer, Newfoundland, West Highland White Terrier, Cocker Spaniel, Beagle, Basset Hound, Airedale Terrier, Boykin Spaniel, Chihuahua, Scottish Terrier, Boxer, Fox Terrier, Chow Chow, Labrador Retriever, Schnauzer

Atrial Septal Defect
Samoyed, Doberman Pinscher, Boxer

Ventricular Septal Defect
English Bulldog, English Springer Spaniel, Keeshond, West Highland White Terrier, cats

Tricuspid Dysplasia
Labrador Retriever, German Shepherd, Boxer, Weimaraner, Great Dane, Old English Sheepdog, Golden Retriever, various other large breeds

Mitral Dysplasia
Bull Terrier, German Shepherd, Great Dane, Golden Retriever, Newfoundland, Mastiff, Rottweiler, cats

Tetralogy of Fallot
Keeshond, English Bulldog

Persistent Right Aortic Arch
German Shepherd, Great Dane, Irish Setter

Cor Triatriatum
Medium- to large-breed dogs (Chow Chow), rarely small-breed dogs or cats

Peritoneopericardial Diaphragmatic Hernia
Weimaraner

Heart Failure

Causes of Chronic Heart Failure

Left-Sided Heart Failure

Volume-Flow Overload
Mitral valve regurgitation (degenerative, congenital, infective)
Aortic regurgitation (infective endocardiosis, congenital)
Ventricular septal defect
Patent ductus arteriosis

Myocardial Failure
Myocardial ischemia/infarction
Drug toxicity (e.g., doxorubicin)

Pressure Overload
Aortic/subaortic stenosis
Systemic hypertension

Restriction of Ventricular Filling
Hypertrophic cardiomyopathy
Restrictive cardiomyopathy

Left- or Right-Sided Heart Failure

Myocardial Failure
Idiopathic dilated cardiomyopathy
Infective myocarditis

Volume-Flow Overload
Chronic anemia
Thyrotoxicosis

Right-Sided Heart Failure

Volume-Flow Overload
Tricuspid endocarditis
Tricuspid endocardiosis
Tricuspid dysplasia

Pressure Overload
Pulmonic stenosis
Heartworm disease
Pulmonary hypertension

Restriction to Ventricular Filling

Cardiac tamponade
Constrictive pericardial disease

Severity

Classification Systems

New York Heart Association Functional Classification

Class I: Heart disease present, but no evidence of heart failure or exercise intolerance; cardiomegaly minimal to absent

Class II: Signs of heart disease with evidence of exercise intolerance; radiographic cardiomegaly present

Class III: Signs of heart failure with normal activity or signs at night (e.g., cough, orthopnea); radiographic signs of significant cardiomegaly and pulmonary edema or pleural/abdominal effusion

Class IV: Severe heart failure with clinical signs at rest or with minimal activity; marked radiographic signs of congestive heart failure (CHF) and cardiomegaly

Forrester Classification

Class I: Normal cardiac output and pulmonary venous pressure

Class II: Pulmonary congestion but normal cardiac output

Class III: Low cardiac output and peripheral hypoperfusion with no pulmonary congestion

Class IV: Low cardiac output with pulmonary congestion

Clinical Findings

Low-Output Signs

Exercise intolerance
Syncope
Weak arterial pulses
Tachycardia
Arrhythmias
Cold extremities
Prerenal azotemia
Cyanosis

Signs Related to Poor Skeletal Muscle Function

Weight loss
Exercise intolerance

Dyspnea
Decreased muscle mass

Signs Related to Fluid Retention

Left-Sided Heart Failure (Pulmonary Edema)

Dyspnea/orthopnea
Exercise intolerance
Wet lung sounds
Tachypnea
Gallop rhythm
Functional mitral regurgitation
Cyanosis
Cough

Right-Sided Heart Failure

Ascites
Subcutaneous edema
Jugular distension/pulsation
Hepatomegaly
Splenomegaly
Hepatojugular reflux
Gallop rhythm
Cardiac arrhythmias

Bilateral Signs

Pleural effusion (dyspnea, muffled heart sounds, cough)

Heartworm Disease

Clinical Findings

Historical Findings

Asymptomatic
Cough
Dyspnea
Weight loss
Lethargy
Exercise intolerance
Poor condition
Syncope
Abdominal distension (ascites)

Physical Findings

Weight loss
Right-sided murmur (tricuspid insufficiency)
Split-second heart sound
Gallop rhythm
Cough

Pulmonary crackles
Dyspnea
Muffled breath sounds
Cyanosis
Right-sided heart failure
- Jugular distension/pulsation
- Hepatosplenomegaly
- Ascites

Pulmonary thromboembolism
- Dyspnea/tachypnea
- Fever
- Hemoptysis

Cardiac arrhythmias/conduction disturbances (rare)
Caval syndrome
- Hemoglobinuria
- Anemia
- Disseminated intravascular coagulation (DIC)
- Icterus
- Collapse/death

Clinicopathologic Findings

Eosinophilia
Nonregenerative anemia
Neutrophilia
Basophilia
Proteinuria
Hyperbilirubinemia
Azotemia
Thrombocytopenia

Radiographic Signs

Right ventricular enlargement
Prominent main pulmonary artery segment
Increased pulmonary artery size
Tortuous pulmonary vessels
Caudal vena cava enlargement
Hepatosplenomegaly
Ascites
Pleural effusion
Bronchial/interstitial lung disease

Diagnosis in Dogs

Antigen Test Positive and Modified Knott's or Filter Test Negative

- Perform complete blood count, serum chemistry panel, urinalysis, thoracic radiography
- Start preventative and adulticidal therapy

- Antigen test positive and Modified Knott's or filter test positive
- Perform complete blood count, serum chemistry panel, urinalysis, and thoracic radiography
- Start "slow kill" macrolide and adulticidal therapy

Antigen Test Negative

- No infection or low heartworm burden
- Start preventative

Hypertension

Pulmonary Hypertension

Potential Clinical Signs

Ascites
Jugular venous distension/pulsation
Subcutaneous edema
Cachexia
Nonspecific respiratory signs

- Coughing
- Tachypnea
- Respiratory distress
- Increased bronchovesicular sounds
- Hemoptysis

Cyanosis

- Right-to-left cardiac shunts
- Severe respiratory disease

Split or loud pulmonic component to second heart sound
Right or left apical systolic murmurs (tricuspid or mitral regurgitation)

Radiographic Signs

Cardiomegaly
Right ventricular enlargement
Dilated central pulmonary arteries with tapering toward periphery
Eisenmenger complex (pulmonary undercirculation and right-sided heart enlargement)
Left atrial enlargement and perihilar to caudodorsal pulmonary infiltrates (left-sided congestive heart failure)

Echocardiographic Signs

Right ventricular concentric hypertrophy and dilation
Main pulmonary artery and main branch dilation
Systolic flattening of interventricular septum

Paradoxical septal motion
Reduced left ventricular dimensions in severe pulmonary hypertension caused by ventricular underfilling

Laboratory Values

Acidosis
Rule out heartworm disease

Systemic Hypertension

Causes of Systemic Hypertension in Dogs and Cats

Renal failure (chronic or acute)
Hyperadrenocorticism
Diabetes mellitus
Pheochromocytoma
Hyperthyroidism
Liver disease
Hyperaldosteronism
Intracranial lesions (↑ intracranial pressure)
High-salt diet
Obesity
Chronic anemia (cats)

Clinical Signs of Systemic Hypertension

Ocular Findings

Hypertensive choroidopathy (edema, vascular tortuosity, hemorrhage, focal ischemia)
Hypertensive retinopathy (edema, vascular tortuosity, hemorrhage, focal ischemia, atrophy)
Intraocular hemorrhage (retinal, vitreal, hyphema)
Papilledema
Blindness
Glaucoma
Secondary corneal ulcers

Neurologic Findings

Edema (↑ intracranial pressure)
Hypertensive encephalopathy (lethargy, behavioral changes)
Cerebrovascular accident (focal ischemia, hemorrhage)
Seizures/collapse

Renal

Polyuria/polydipsia
Glomerulosclerosis/proliferative glomerulitis
Renal tubular degenerative and fibrosis
Further deterioration in renal function

Cardiac

Left ventricular hypertrophy
Murmur or gallop sound
Aortic dilation
Aneurysm or dissection rare

Other

Epistaxis

Laryngeal and Pharyngeal Disease

Differential Diagnosis

Laryngeal paralysis
Brachycephalic airway syndrome
Acute laryngitis
Laryngeal neoplasia
Nasopharyngeal polyp
Abscess
Tonsillitis
Pharyngitis
Obstructive laryngitis
Laryngeal collapse
Trauma
Foreign body
Extraluminal mass
Elongated soft palate
Cleft palate
Soft palate hypoplasia
Pharyngeal neoplasia
Granuloma
Pharyngeal mucoceles
Web formation
Nasopharyngeal stenosis

Causes of Laryngeal Paralysis

Idiopathic

Polyneuropathy and Polymyopathy

Idiopathic
Immune-mediated
Endocrinopathy
- Hypothyroidism
- Hypoadrenocorticism

Toxicity
Congenital disease

Ventral Cervical Lesion

Nerve trauma
- Direct trauma
- Inflammation
- Fibrosis

Neoplasia
Other inflammatory or mass lesion

Anterior Thoracic Lesion

Neoplasia
Trauma
- Postoperative
- Other

Other inflammatory or mass lesion

Myasthenia Gravis

Lower Respiratory Tract Disease

Differential Diagnosis

Disorders of Trachea and Bronchi

Canine infectious tracheobronchitis
Collapsing trachea
Bacterial infection
Mycoplasmal infection
Bronchial asthma
Neoplasia
Allergic bronchitis
Feline bronchitis
Bronchial compression
- Left atrial enlargement
- Hilar lymphadenopathy

Acute bronchitis
Canine chronic bronchitis/bronchiectasis
Parasites *(Oslerus osleri, Filaroides osleri)*
Tracheal tear
Primary ciliary dyskinesia
Airway foreign body
Chronic aspiration

Disorders of Pulmonary Parenchyma

Infectious disease
- Viral pneumonia (canine influenza, canine distemper virus, canine adenovirus, canine parainfluenza, feline calicivirus, feline infectious peritonitis, pneumonia secondary to feline leukemia virus or feline immunodeficiency virus)

- Bacterial pneumonia
- Protozoal pneumonia (toxoplasmosis)
- Fungal pneumonia (blastomycosis, histoplasmosis, coccidioidomycosis)
- Rickettsial disease (*Rickettsia rickettsii, Ehrlichia* spp.)
- Parasitism
  - Heartworm disease
  - Pulmonary parasites (*Paragonimus, Aelurostrongylus, Capillaria, Crenosoma* spp.)
  - Larval migration of *Toxocara canis*

Aspiration pneumonia
Pulmonary infiltrates with eosinophils
Eosinophilic pulmonary granulomatosis
Aspiration pneumonia
Pulmonary neoplasia (primary, metastatic, lymphosarcoma, lymphomatoid granulomatosis, malignant histiocytosis)
Pulmonary hypertension
Pulmonary contusions
Pulmonary thromboembolism
Pulmonary edema
Acute respiratory distress syndrome
Lung lobe torsion
Pulmonary fibrosis
Pickwickian syndrome (obesity)
Idiopathic interstitial pneumonias

Mediastinal Disease

Differential Diagnosis of Lesions Associated with Focal Mediastinal Enlargement

Pneumomediastinum
Mediastinitis (*Histoplasma, Cryptococcus, Actinomyces, Nocardia, Spirocerca* spp.)
Mediastinal hemorrhage
Mediastinal cysts
Nonneoplastic mediastinal masses (fungal pyogranulomas, abscesses, granulomas, lymphadenopathy, hematomas)
Mediastinal neoplasia (lymphosarcoma)
Thymoma
Obesity
Thymic hemorrhage
Heart base mass
Neurogenic tumor
Tracheal mass
Esophageal mass, foreign body, or dilatation

Ectopic thyroid tissue
Mediastinal edema
Vascular mass (aorta, cranial vena cava)
Paraspinal or spinal mass
Aortic stenosis
Patent ductus arteriosus
Left atrial enlargement
Main pulmonary artery mass (poststenotic dilatation)
Hiatal hernia
Diaphragmatic hernia or mass
Aortic aneurysm
Gastroesophageal intussusception
Peritoneopericardial diaphragmatic hernia

Myocardial Diseases

Differential Diagnosis, Dogs

Dilated Cardiomyopathy

Primary (idiopathic, most common)

Genetic (Doberman Pinscher, Boxer, Cocker Spaniel, Great Dane, Portuguese Water Dog, Newfoundland, Dalmatian, Irish Wolfhound)

Secondary

Nutritional Deficiencies

L-Carnitine (Boxer, Doberman Pinscher, Great Dane, Irish Wolfhound, Newfoundland, Cocker Spaniel)
Taurine

Myocardial Infection

Viral myocarditis (acute viral infections, e.g., parvovirus)
Bacterial myocarditis (secondary to bacteremia from infections elsewhere in body)
Lyme disease: *Borrelia burgdorferi*
Protozoal myocarditis *(Trypanosoma cruzi [Chagas disease], Toxoplasma gondii, Neospora caninum, Babesia canis, Hepatozoon canis)*
Fungal myocarditis (rare, *Aspergillus, Cryptococcus, Coccidioides, Histoplasma, Paecilomyces* spp.)
Rickettsial myocarditis (rare, *Rickettsia rickettsii, Ehrlichia canis, Bartonella* spp.)
Algae-like organisms (rare, *Prototheca* spp.)
Nematode larval migration (*Toxocara* spp.)

Trauma

Ischemia

Infiltrative Neoplasia

Hyperthermia

Irradiation

Electric Shock

Cardiotoxins

Doxorubicin; ethyl alcohol; plant toxins such as foxglove, black locust, buttercup, lily of the valley, and gossypol; cocaine; anesthetic drugs; catecholamines; monensin

Hypertrophic Cardiomyopathy (uncommon in dogs)

Arrhythmogenic Right Ventricular Cardiomyopathy (rare)

Noninfective Myocarditis

Catecholamines; heavy metals; antineoplastic drugs (doxorubicin, cyclophosphamide, 5-fluorouracil, interleukin-2, interferon-α); stimulant drugs (thyroid hormone, cocaine, amphetamines, lithium)

Immune-mediated diseases, pheochromocytoma

Wasp and scorpion stings, snake venom, spider bite

Differential Diagnosis, Cats

Hypertrophic Cardiomyopathy

Primary (Idiopathic)

Maine Coon, Persian, Ragdoll, and American shorthair may be predisposed.

Secondary

Hyperthyroidism

Hypersomatotropism (acromegaly)

Infiltrative myocardial disease (lymphoma)

Restrictive Cardiomyopathy

Dilated Cardiomyopathy

Taurine-deficient diets

Doxorubicin

End stage of other myocardial metabolic, toxic, or infectious process

Arrhythmogenic Right Ventricular Cardiomyopathy

Myocarditis

Viral (coronavirus, other viruses)

Bacterial (bacteremia, *Bartonella* spp.)
Protozoal *(Toxoplasma gondii)*

Murmurs

Clinical Findings

Systolic Murmurs

Functional murmurs (point of maximal impulse [PMI] over left-sided heart base, decrescendo or crescendo-decrescendo)

- Innocent puppy murmurs
- Physiologic murmurs (anemia, fever, high sympathetic tone, hyperthyroidism, peripheral arteriovenous fistula, marked bradycardia, hypoproteinemia, athletic heart)

Mitral valve insufficiency (left apex, typically holosystolic)

Ejection murmurs (typically left-sided heart base)

- Subaortic stenosis (low left base and right base)
- Pulmonic stenosis (high left base)
- Dynamic muscular obstruction

Right-sided murmurs (usually holosystolic)

- Tricuspid insufficiency (right apex, may see jugular pulse)
- Ventricular septal defect (PMI over right sternal border)

Diastolic Murmurs

Aortic insufficiency from bacterial endocarditis (left-sided heart base)
Aortic valve congenital malformations (left base)
Aortic valve degenerative disease (left base)
Pulmonic insufficiency (left base)

Continuous Murmurs

Patent ductus arteriosus (PMI high left base above pulmonic area)

Concurrent Systolic and Diastolic Murmurs (To-and-Fro Murmurs)

Subaortic stenosis with aortic insufficiency
Pulmonic stenosis with pulmonic insufficiency

Grading

Grade I: Very soft murmur; heard only in quiet surroundings after minutes of listening

Grade II: Soft murmur but easily heard
Grade III: Moderate-intensity murmur
Grade IV: Loud murmur; no precordial thrill
Grade V: Loud murmur with palpable precordial thrill
Grade VI: Very loud murmur; can be heard with stethoscope off chest wall; palpable precordial thrill

Pericardial Effusion

Differential Diagnosis

Bacterial Pericarditis
- Secondary to foxtail (*Hordeum* spp.) migration
- Secondary to penetrating animal bite
- Disseminated tuberculosis

Fungal Pericarditis
- Coccidioidomycosis
- Aspergillosis
- Actinomycosis

Viral Pericarditis
- Feline infectious peritonitis (FIP)
- Canine distemper virus

Protozoal Pericarditis
- Toxoplasmosis
- Other systemic protozoal infections

Left Atrial Rupture (Secondary to Mitral Valve Disease)

Neoplasia
- Hemangiosarcoma
- Mesothelioma
- Heart base tumor (aortic body tumor or chemodectoma, ectopic thyroid tumor, ectopic parathyroid tumor, connective tissue neoplasms)
- Lymphosarcoma
- Rhabdomyosarcoma

Other
- Penetrating trauma
- Pericardioperitoneal diaphragmatic hernia
- Hypoalbuminemia
- Pericardial cyst
- Coagulation disorders
- Congestive heart failure
- Uremia
- Idiopathic

Pleural Effusion

Differential Diagnosis

Transudates and Modified Transudates

- Right-sided heart failure
- Pericardial disease
- Hypoalbuminemia
- Neoplasia
- Diaphragmatic hernia

Nonseptic Exudates

- Feline infectious peritonitis (FIP)
- Neoplasia
- Diaphragmatic hernia
- Lung lobe torsion

Septic Exudates

- Pyothorax

Chylous Effusion

- Chylothorax

Hemorrhage

- Trauma
- Bleeding disorder
- Neoplasia
- Lung lobe torsion

Diagnostic Approach in Dogs and Cats with Pleural Effusion Based on Fluid Type

Pure and Modified Transudates

- Right-sided heart failure, pericardial effusion (evaluate pulses, auscultation, ECG, thoracic radiography, echocardiography)
- Hypoalbuminemia (serum albumin concentration)
- Neoplasia, diaphragmatic hernia (thoracic radiography, thoracic ultrasound, CT, thoracoscopy, thoracotomy)

Nonseptic Exudates

- Feline infectious peritonitis (pleural fluid cytology [most reliable test], CBC, serum chemistry, ophthalmoscopic examination, serum or fluid electrophoresis, coronavirus antibody titer, PCR of tissues or effusion)
- Neoplasia, diaphragmatic hernia (thoracic radiography, thoracic ultrasound, CT, thoracoscopy, thoracotomy)
- Lung lobe torsion (thoracic radiography, ultrasound, bronchoscopy, thoracotomy)

Septic Exudates

Pyothorax (Gram stain, aerobic and anaerobic culture, cytology)

Chylous Effusion

Chylothorax (protein concentration, nucleated cell count, cytology, triglyceride)

Hemorrhagic

Trauma (history)
Bleeding disorder (systemic examination, coagulation tests platelet count)
Neoplasia (thoracic radiography, thoracic ultrasound, CT, thoracoscopy, thoracotomy)
Lung lobe torsion (thoracic radiography, ultrasound, bronchoscopy, thoracotomy)

Pulmonary Disease

Differential Diagnosis Based on Radiographic Patterns

Alveolar Pattern

Pulmonary edema (cardiogenic or noncardiogenic)
Infectious pneumonia (bacterial, parasitic, protozoal, viral)
Aspiration pneumonia
Atelectasis
Drowning
Smoke inhalation
Hemorrhage

- Neoplasia (primary and metastatic)
- Fungal pneumonia (severe)
- Pulmonary contusion
- Thromboembolic disease
- Systemic coagulopathy

Bronchial Pattern

Feline bronchitis/asthma
Allergic bronchitis
Bacterial bronchitis
Canine chronic bronchitis
Bronchiectasis
Pulmonary parasites
Bronchial calcification

Vascular Pattern

Enlarged Arteries

Heartworm disease

Thromboembolic disease
Pulmonary hypertension

Enlarged Veins

Left-sided heart failure

Enlarged Arteries and Veins (Pulmonary Overcirculation)

Left-to-Right Shunts

Patent ductus arteriosus
Ventricular septal defect
Atrial septal defect

Small Arteries and Veins

Pulmonary Undercirculation

Cardiovascular shock
Hypovolemia
- Severe dehydration
- Blood loss
- Hypoadrenocorticism

Pulmonic valve stenosis

Hyperinflation of Lungs

Feline bronchitis
Allergic bronchitis

Nodular Interstitial Pattern

Mycotic infection
- Blastomycosis
- Histoplasmosis
- Coccidioidomycosis

Neoplasia
Pulmonary parasites
- Aelurostrongylus infection
- Paragonimus infection

Pulmonary abscess
- Bacterial pneumonia
- Foreign body

Pulmonary infiltrates with eosinophils
Miscellaneous inflammatory diseases
Inactive lesions

Reticular Interstitial Patterns

Infection
- Viral pneumonia
- Bacterial pneumonia
- Toxoplasmosis
- Mycotic pneumonia

Parasitic infestation
Neoplasia

Pulmonary fibrosis
Pulmonary infiltrates with eosinophils
Miscellaneous inflammatory diseases
Hemorrhage (mild)
Old dog lung

Pulmonary Edema

Causes

Vascular Overload

Cardiogenic
- Left-sided heart murmur
- Left-to-right shunt

Overhydration

Decreased Plasma Oncotic Pressure

Hypoalbuminemia
- Gastrointestinal loss
- Renal loss (glomerular disease)
- Liver disease (lack of production)
- Iatrogenic overhydration

Increased Vascular Permeability

Sepsis
Shock
Drugs or toxins
Snake envenomation
Cisplatin (cats)
Trauma
- Pulmonary
- Multisystemic

Inhaled toxins
- Smoke inhalation
- Gastric acid aspiration
- Oxygen toxicity

Electrocution
Pancreatitis
Uremia
Virulent babesiosis
Disseminated intravascular coagulation
Inflammation/Vasculitis

Other Causes

Thromboembolism
Postobstruction (strangulation, laryngeal paralysis, pulmonary reexpansion)
Near-drowning

Neurogenic edema
- Seizures
- Head trauma

Lung lobe torsion
Bacterial pneumonia
Pulmonary contusion
Hyperoxia
High altitude
Air embolus
Pheochromocytoma

Lymphatic Obstruction (rare)
Neoplasia

Pulmonary Thromboembolism

Causes

Embolization of Thrombi (any condition that predisposes to venous stasis, endothelial injury, and hypercoagulability)
Heartworm disease
Immune-mediated hemolytic anemia
Systemic inflammatory disease
Neoplasia
Cardiac disease
Cardiomyopathy
Endocarditis
Congestive heart failure
Protein-losing nephropathy
Protein-losing enteropathy
Hyperadrenocorticism
Pancreatitis
Disseminated intravascular coagulation
Anatomic abnormality (e.g., aneurysm, A-V fistula)
Hyperviscosity (polycythemia, leukemia, hyperglobulinemia)
Hypoviscosity (anemia)
Sepsis
Shock
Intravenous catheterization
Injection of irritating substance
Prolonged recumbency
Reperfusion injury
Atherosclerosis/Arteriosclerosis
Trauma
Recent surgery
Hyperhomocysteinemia

Embolization of Parasites
Heartworm disease

Embolization of Fat

Embolization of Neoplastic Cells

Tachycardia, Sinus

Causes

Anxiety/fear
Excitement
Exercise
Pain
Hyperthyroidism
Hyperthermia/fever
Anemia
Hypoxia
Shock
Hypotension
Sepsis
Drugs (anticholinergics, sympathomimetics)
Toxicity (e.g., chocolate, hexachlorophene)
Electric shock

SECTION II

Dermatologic Disorders

Allergic Skin Disease

Clinical Findings

Flea Allergy

Dogs

Papular rash
Caudal distribution of lesions most common

Cats

Miliary dermatitis, especially over caudal back, around neck and chin
Eosinophilic granuloma complex

Atopy and Cutaneous Signs of Food Hypersensitivity

Signs of these two types of allergy are similar.
Atopy tends to occur primarily in young adults, whereas food hypersensitivity can begin at any age. Atopy is usually seasonal at first but may become less seasonal.

Dogs

Papular rash
Pruritus and self-trauma
Lesions of face, ears, feet, and perineum
Recurrent otitis externa
Excoriation
Lichenification
Pigmentary changes
Secondary pyoderma

Cats

Miliary dermatitis
Eosinophilic dermatitis

Allergic Contact Dermatitis

Rarest of allergic dermatoses
Lesions tend to be confined to hairless or sparsely haired skin (ventral abdomen, neck, and chest; ventral paws but not pads; perineum; lateral aspect of pinnae).
Acutely: Erythema, macules, papules, vesicles
Chronically: Alopecic plaques, hyperpigmentation, hypopigmentation, excoriation, lichenification

Alopecia, Endocrine

Causes

Hypothyroidism
Hyperadrenocorticism
Diabetes mellitus
Adrenal sex hormone deficiency (Alopecia X)
Growth hormone deficiency (pituitary dwarfism)
Growth hormone-responsive dermatosis in adult dogs
Castration-responsive dermatosis
Hyperestrogenism
- Sertoli cell tumor (male dog)
- Intact female dog

Hypoestrogenism (poorly understood)
- Estrogen-responsive dermatosis of spayed female dogs
- Feline endocrine alopecia

Hypoandrogenism
- Testosterone-responsive dermatosis (male dog)
- Feline endocrine alopecia

Telogen defluxion (effluvium): often after recent pregnancy or diestrus
Progestin excess (excess of progesterone or 17-hydroxyprogesterone)

Clinical Findings

Nonspecific Features of Endocrine Disease

Bilaterally symmetric alopecia
Follicular dilation, follicular keratosis, follicular atrophy
Orthokeratotic hyperkeratosis
Predominance of telogen hair follicles
Sebaceous gland atrophy
Epidermal atrophy
Thin dermis
Epidermal melanosis
Dermal collagen atrophy

Features Suggestive of Specific Endocrine Disorder

Hypothyroidism
- Vacuolated and/or hypertrophied arrector pili muscles, increased dermal mucin content, thick dermis

Hyperadrenocorticism
- Calcinosis cutis, comedones, absence of erector pili muscles

Hyposomatotropism
- Decreased amount and size of dermal elastin fibers

Growth hormone and castration-responsive dermatoses
- Excessive trichilemmal keratinization (flame follicles)

Claw Disorders

Differential Diagnosis for Abnormal Claws

Bacterial Claw Infection—almost always secondary to an underlying cause
- Trauma—usually one claw affected
- Hypothyroidism
- Hyperadrenocorticism
- Allergies
- Autoimmune disorders
- Symmetrical lupoid onychodystrophy
- Neoplasia

Fungal Claw Infection
- Typically caused by dermatophytes

Symmetrical Lupoid Onychodystrophy
- Suspected to be immune mediated. German shepherds and Rottweilers may be predisposed. Acute onset of claw loss, initially 1-2 but eventually all claws slough. Replacement claws are misshapen, soft or brittle, discolored, and friable and usually slough again. Feet are painful and pruritic. Paronychia is uncommon unless secondary bacterial infection is present.

Drug Eruption

Vasculitis

Diagnostic Tests for Abnormal Claws

- Cytology—suppurative to pyogranulomatous inflammation with bacteria
- Bacterial culture of exudates from claw or claw fold. Mixed infections common. *Staphylococcus* spp. usually isolated
- Fungal culture—*Trichophyton* spp. most commonly isolated but may also see *Microsporum* spp. or *Malassezia* spp.
- Radiography—rule out osteomyelitis

- Dermatohistopathology—(P3 amputation), only recommended to rule out neoplasia. With symmetric lupoid onychodystrophy, see basal cell hydropic degeneration, degeneration or apoptosis of individual keratinocytes in the basal layer, pigmentary incontinence, and lichenoid interface dermatitis. Systemic lupoid onychodystrophy is most commonly diagnosed by typical history and clinical signs along with ruling out other differentials.

Erosions and Ulcerations of Skin or Mucous Membranes

Differential Diagnosis, Dogs

Excoriation from Any Pruritic Skin Disease

Infection

Bacterial Pyoderma

Surface (pyotraumatic moist dermatitis, intertrigo)
Deep (folliculitis, furunculosis, bacterial stomatitis)

Fungal

Yeast infection (*Malassezia pachydermatis, Candida* spp.)
Dermatophytosis
Systemic fungal infection (blastomycosis, coccidioidomycosis, cryptococcosis, histoplasmosis, others)
Subcutaneous mycoses (pythiosis, zygomycosis, phaeohyphomycosis, sporotrichosis, eumycotic mycetoma, others)

Parasitic

Demodicosis

Neoplasia

Squamous cell carcinoma
Epitheliotrophic lymphoma

Metabolic Derangements

Uremia/renal failure
Necrolytic migratory erythema
Calcinosis cutis (hyperadrenocorticism)

Physical/Chemical Injury

Drug reactions
Urine scald
Thermal injury (burn, freeze)
Solar injury

Immune-Mediated Disorders

Discoid lupus erythematosus (DLE)
Pemphigus

Uveodermatologic syndrome
Miscellaneous autoimmune subepidermal vesiculobullous diseases (bullous pemphigoid, epidermolysis acquisita, linear IgA bullous disease, mucocutaneous pemphigoid, bullous systemic lupus type 1)

Miscellaneous
Arthropod bites
Dermatomyositis
Dystrophic epidermolysis bullosa, junctional epidermolysis bullosa
Idiopathic ulceration of Collies
Toxic epidermal necrolysis, erythema multiforme

Differential Diagnosis, Cats

Infection

Viral
Calicivirus
Herpesvirus

Bacterial
Atypical mycobacteriosis

Fungal
Cryptococcosis
Systemic and subcutaneous mycoses
Sporotrichosis

Neoplasia
Squamous cell carcinomas (especially white, outdoor cats)
Fibrosarcoma
Cutaneous lymphoma

Metabolic Derangements
Uremia/renal disease

Physical/Chemical Injury
Thermal
Drug reactions

Immune-Mediated Disorders
Bullous pemphigoid
Pemphigus foliaceus
Plasma cell pododermatitis
Toxic epidermal necrolysis

Inflammatory/Allergic Disorders
Eosinophilic plaque
Indolent ulcer
Arthropod bites

Miscellaneous/Idiopathic
Dystrophic epidermolysis bullosa
Idiopathic ulceration of dorsal neck
Junctional epidermolysis bullosa

Folliculitis

Differential Diagnosis

Superficial Folliculitis
Inflammation of hair follicles
- Bacterial pyoderma
- Fungal (dermatophytosis)
- Parasitic (demodicosis, *Pelodera* dermatitis)

Deep Folliculitis/Furunculosis
Inflammation of hair follicles with subsequent follicular rupture into dermis and subcutaneous tissues
- Deep pyodermas

Otitis Externa, Chronic

Primary Causes

Allergy
Atopy
Adverse reactions to foods
Contact dermatitis

Parasites
Otodectes cynotis
Notoedres cati
Sarcoptes scabiei
Demodex spp.
Chiggers
Flies
Ticks (spinous ear tick)

Dermatophytes

Endocrine Disorders
Hypothyroidism

Foreign Bodies
Foxtails, hair, etc.

Glandular Conditions
Ceruminous gland hyperplasia
Sebaceous gland hyperplasia or hypoplasia
Altered type or rate of secretions

Autoimmune Diseases
- Systemic lupus erythematosus (SLE)
- Pemphigus foliaceus/erythematosus
- Cold agglutinin disease
- Juvenile cellulitis

Viruses
- Distemper

Miscellaneous
- Solar dermatitis
- Frostbite
- Vasculitis/vasculopathy
- Eosinophilic dermatitis
- Sterile eosinophilic folliculitis
- Relapsing polychondritis

Predisposing Factors

Conformation
- Stenotic canals
- Hair in canals
- Pendulous pinnae
- Hairy, concave pinna

Excessive Moisture
- Swimmer's ear
- High-humidity climate

Excessive Cerumen Production
- Secondary to underlying disease
- Primary (idiopathic)

Treatment Effects
- Trauma from cotton swabs
- Topical irritants
- Superinfections from altering microflora

Obstructive Ear Disease
- Polyps
- Granulomas
- Tumors

Systemic Disease
- Immunosuppression
- Debilitation
- Negative catabolic states

Perpetuating Factors

Bacteria (most commonly *Staphylococcus* spp., *Streptococcus* spp., *Pseudomonas* spp., *Proteus*, *Escherichia coli*)

Yeast *(Malassezia pachydermatis)*

Progressive Pathologic Changes
- Hyperkeratosis
- Hyperplasia
- Epithelial folds
- Apocrine gland hypertrophy
- Hidradenitis
- Fibrosis

Otitis Media
- Purulent
- Caseated or keratinous
- Cholesteatoma
- Proliferative
- Destructive osteomyelitis

Parasitic Dermatoses

Classification

Fleas (*Ctenocephalides felis* most common)
- Flea infestation
- Flea allergy dermatitis
  - Caudal distribution of lesions (dogs)
  - Miliary dermatitis (cats)

Demodicosis
- Follicular infection *(Demodex canis, Demodex felis)*
- Epidermal infection (*Demodex gatoi,* short-tailed demodectic mite of dogs)

Sarcoptic Mange
- *Sarcoptes scabiei* (dogs, rarely cats)
- *Notoedres cati* (cats, rarely dogs)

Ear Mites
- *Otodectes cynotis* (common in both dogs and cats)

Cheyletiellosis
- *Cheyletiella yasguri* (primary host is dogs)
- *C. blakei* (primary host is cats)

C. parasitovorax (primary host is rabbits)
All *Cheyletiella* species freely contagious from one species to another

Chiggers
Larval stage (six-legged bright red or orange) is the parasitic stage; nymph and adult are free living.

Ticks
Brown dog tick *(Rhipicephalus sanguineus)*
American dog tick *(Dermacentor variabilis)*
Rocky Mountain wood tick *(Dermacentor andersoni)*
Lone star tick *(Amblyomma americanum)*
Deer tick *(Ixodes dammini):* primary vector of *Borrelia burgdorferi*
Spinous ear tick *(Otobius megnini)*

Lice
Sucking lice of dogs *(Linognathus setosus)*
Biting lice of dogs *(Trichodectes canis, Heterodoxus springer)*
Lice of cats *(Felicola subrostrata)*

Insects of Order Diptera
Mosquitoes: eosinophilic dermatitis (especially cats)
Black flies, stable flies, horn flies, houseflies: attack ear pinnae of dogs
Myiasis (development of fly larvae in skin or haircoat): screwworm, blow flies, flesh flies
Cuterebra fly larva

Helminth Parasites
Hookworm dermatitis *(Ancylostoma, Uncinaria)*
Pelodera dermatitis *(Peloderma strongyloides)*
Dracunculiasis *(Dracunculus insignis)*

Pigmentation

Differential Diagnosis for Changes in Skin Pigmentation

Hypopigmentation
Vitiligo (Tervuren, Rottweiler, Doberman Pinscher, Newfoundland, Collie, German Shorthaired Pointer, Old English Sheepdog, Siamese cat)
Uveodermatologic syndrome (northern breeds such as Siberian Husky, Samoyed, Akita)
Acquired idiopathic hypopigmentation of nose (Labrador Retriever, Golden Retriever, Malamute, Siberian Husky, Samoyed, Poodle, German Shepherd)

Discoid lupus (German Shepherd, Collie, others)
Dermatomyositis (Collie, Shetland Sheepdog, Beauceron Shepherd)

Hyperpigmentation

Postinflammatory Hyperpigmentation

Any Chronic Pruritic Skin Disease
Atopy
Adverse food reactions
Pyoderma
Malassezia dermatitis
Sarcoptic mange
Erythema multiforme
Many others

Demodicosis

Endocrinopathies

Hypothyroidism
Hyperadrenocortism

Dermatophytosis

Nevus

Lentigo

Neoplasia (melanoma)

Pyoderma

Differential Diagnosis

Surface Pyoderma

Pyotraumatic dermatitis (acute moist dermatitis, "hot spot")
Intertrigo (skin fold dermatitis)

Superficial Pyoderma

Impetigo (subcorneal pustules of sparsely haired skin)
- Puppy pyoderma

Bullous impetigo
- Hyperadrenocorticism, hypothyroidism, diabetes mellitus

Mucocutaneous pyoderma
- Dogs (German Shepherds predisposed)

Superficial bacterial folliculitis
- Staphylococcus pseudintermedius most common
- Local trauma secondary to pruritus (allergy, fleas, scabies, demodicosis, etc.)

Dermatophilosis (rare, actinomycotic superficial crusting dermatitis) methicillin-resistant *Staphylococcus pseudintermedius*

Deep Pyoderma

Always secondary to predisposing problem
Localized lesion (laceration, penetrating wound, animal bite, foreign body)
Generalized (suspect underlying systemic disease)
Clinical syndromes associated with deep pyoderma

- Deep folliculitis, furunculosis, cellulitis
- Pyotraumatic folliculitis
- Muzzle folliculitis and furunculosis
- Pododermatitis (interdigital pyoderma)
- German Shepherd dog folliculitis, furunculosis, cellulitis
- Acral lick furunculosis
- Anaerobic cellulites
- Subcutaneous abscesses
- Bacterial pseudomycetoma
- Mycobacterial granulomas
  - Cutaneous tuberculosis (*Mycobacterium tuberculosis, M. bovis*)
  - Feline leprosy (*M. lepraemurium*)
  - Opportunistic mycobacterial granulomas
- Actinomycosis
- Actinobacillosis
- Nocardiosis

Miscellaneous Bacterial Infections

Brucellosis, plague, borreliosis, *trichomycosis axillaris*, L-form infections

Endocrinologic and Metabolic Disorders

Acromegaly

In dogs, acromegaly is caused by endogenous progesterone from the luteal phase of the estrous cycle or by exogenous progesterone used for estrous prevention. Elevated progesterone, in turn, stimulates excessive growth hormone secretion of mammary origin. In cats, acromegaly is caused by a pituitary adenoma, usually a macroadenoma, which secretes excessive amounts of growth hormone. Physical changes are less pronounced in cats than in dogs.

Clinical Findings, Dogs

Hypertrophy of mouth, tongue, and pharynx
Thick skin folds, myxedema, hypertrichosis
Prognathism
Wide interdental spacing
Visceral organomegaly
Insulin-resistant diabetes mellitus
Polyuria
Polyphagia
Elevated alkaline phosphatase

Clinical Findings, Cats

Physical changes most pronounced on head, but all the physical changes listed for dogs may be seen.
Insulin-resistant diabetes mellitus (severe)
Degenerative arthropathy/lameness
Polyuria/polydipsia
Polyphagia
Panting
Lethargy/exercise intolerance
Dyspnea secondary to hypertrophic cardiomyopathy and heart failure
Neurologic signs when macroadenoma becomes large

- Lethargy, stupor
- Adipsia
- Anorexia
- Temperature deregulation
- Circling
- Seizures
- Pituitary dysfunction
  - Hypogonadism
  - Hypothyroidism
  - Hypoadrenocorticism (feline acromegaly may also coexist with pituitary-dependent hyperadrenocorticism)

Adrenal Tumors

Differential Diagnosis

Nonfunctional Adrenal Tumor (dog, rarely cat)
No hormone secreted
Diagnosis by exclusion
Histopathology

Functional Adrenocortical Tumor

Cortisol-Secreting Tumor
Hyperadrenocorticism (Cushing syndrome) (dog, rarely cat)
Diagnosis by adrenocorticotropic hormone (ACTH) stimulation test, low-dose dexamethasone suppression test, adrenal ultrasound, CT scan

Aldosterone-Secreting Tumor
Hyperaldosteronism (Conn syndrome) (cat, rarely dog)
Diagnosis by assessing Na/K, ACTH stimulation test (measure aldosterone)

Progesterone-Secreting Tumor
Mimics hyperadrenocorticism (cat, less commonly dog)
Diagnosis by measuring serum progesterone

Steroid Hormone Precursor–Secreting Tumor

17-hydroxyprogesterone
Mimics hyperadrenocorticism (dog)
Diagnosis by ACTH stimulation test (measure steroid hormone precursors)
Deoxycorticosterone
Mimics hyperadrenocorticism (dog)
Diagnosis by ACTH stimulation test (measure steroid hormone precursors)

Functional Adrenomedullary Tumor

Epinephrine-Secreting Tumor

Pheochromocytosis (dog, rarely cat)
Diagnosis by exclusion, histopathology

Cretinism (Hypothyroidism in Puppies)

Clinical Findings

Dwarfism
Short, broad skull with short thick neck
Enlarged cranium
Shortened limbs
Shortened mandible
Mental dullness
Alopecia
Retention of puppy coat
Kyphosis
Inappetence
Hypothermia
Constipation
Gait abnormalities
Delayed dental eruption
Macroglossia
Dry coat
Thick skin
Lethargy
Dyspnea
Goiter

Diabetes Insipidus

Differential Diagnosis

Features of diabetes insipidus include polyuria, polydipsia, and a near-continuous demand for water. Only the following three disorders can cause the degree of polyuria and dilute urine seen with diabetes insipidus:

- Central diabetes insipidus
- Nephrogenic diabetes insipidus
- Primary polydipsia

Causes in Dogs and Cats

Central Diabetes Insipidus

Idiopathic
Traumatic
Neoplasia
- Primary pituitary neoplasm
- Meningioma
- Craniopharyngioma
- Chromophobe adenoma
- Chromophobe adenocarcinoma
- Metastatic neoplasia

Pituitary malformation
Cysts
Inflammation
Parasitic lesions
Complication of pituitary surgery
Familial?

Nephrogenic Diabetes Insipidus

Polyuria caused by nonresponsiveness to antidiuretic hormone (ADH).
Primary idiopathic
Primary familial (Husky)
Secondary acquired
- Renal insufficiency or failure
- Hyperadrenocorticism
- Hypoadrenocorticism
- Hepatic insufficiency
- Pyometra
- Hypercalcemia
- Hypokalemia
- Postobstructive diuresis
- Diabetes mellitus
- Normoglycemic glucosuria
- Hyperthyroidism
- Iatrogenic or drug induced
- Renal medullary solute washout

Diabetic Ketoacidosis

Clinical Findings

No signs may be seen early with diabetic ketoacidosis.

Historical Findings

Lethargy
Anorexia
Vomiting

Physical Examination Findings

Dehydration
Depression
Weakness
Tachypnea
Vomiting
Acetone odor on breath
Slow, deep breaths (secondary to metabolic acidosis)
Abdominal pain/abdominal distension secondary to concurrent pancreatitis

Clinicopathologic Findings

Hyperglycemia
Metabolic acidosis
Hypercholesterolemia/lipemia
Increased alkaline phosphatase (ALP)
Increased alanine aminotransferase (ALT)
Increased blood urea nitrogen (BUN)/creatinine
Hyponatremia
Hypochloremia
Hypokalemia
Increased amylase/lipase
Hyperosmolality
Glycosuria
Ketonuria
Urinary tract infection

Diabetes Mellitus

Potential Factors in Etiopathogenesis

Obesity
Pancreatitis
Immune-mediated insulitis
Concurrent hormonal disease
- Hyperadrenocorticism
- Diestrus-induced excess of growth hormone
- Hypothyroidism

Genetics (dog, possibly cat)
Drugs
- Glucocorticoids
- Megestrol acetate (cat)

Infection

Concurrent illness
- Renal insufficiency
- Cardiac disease

Hyperlipidemia (dog, possibly cat)
Islet amyloidosis

Clinicopathologic Abnormalities, Uncomplicated Diabetes Mellitus

Complete Blood Count
Often normal
Leukocytosis if pancreatitis or infection present

Serum Chemistry
Hyperglycemia
Mild increase in alkaline phosphatase (ALP) and alanine aminotransferase (ALT)
Hypercholesterolemia/hypertriglyceridemia

Urinalysis
Urine specific gravity normal to mildly decreased (>1.025)
Glycosuria
Variable ketonuria
Bacteriuria
Proteinuria

Ancillary Tests
Increased amylase/lipase if pancreatitis present
Normal serum trypsin-like immunoreactivity (TLI)
Low TLI with exocrine pancreatic insufficiency
High TLI with acute pancreatitis
Normal to high TLI with chronic pancreatitis
Low to normal serum insulin with insulin-dependent diabetes mellitus
Low, normal, or increased serum insulin with non–insulin-dependent diabetes mellitus

Potential Complications

Common
Iatrogenic hypoglycemia
Polyuria/polydipsia
Weight loss
Cataracts (dog)
Anterior uveitis
Bacterial infections (especially urinary tract infection)
Ketoacidosis
Pancreatitis
Peripheral neuropathy (cat)
Hepatic lipidosis

Uncommon

- Peripheral neuropathy (dog)
- Glomerulopathy
- Glomerulosclerosis
- Retinopathy
- Exocrine pancreatic insufficiency
- Gastric paresis
- Diabetic diarrhea
- Diabetic dermatopathy

Causes of Insulin Resistance or Ineffectiveness in Dogs and Cats

Caused by Insulin Therapy

- Improper administration
- Inadequate dose
- Inactive insulin
- Diluted insulin
- Somogyi effect
- Inappropriate insulin administration
- Impaired insulin absorption
- Antiinsulin antibody excess

Caused by Concurrent Disorder

- Obesity
- Diabetogenic drugs
- Hyperadrenocorticism
- Hypothyroidism (dog)
- Hyperthyroidism (cat)
- Urinary tract infection
- Oral infections
- Chronic inflammation/pancreatitis
- Diestrus (bitch)
- Acromegaly (cat)
- Renal insufficiency
- Hepatic insufficiency
- Cardiac insufficiency
- Glucagonoma
- Pheochromocytoma
- Exocrine pancreatic insufficiency
- Hyperlipidemia
- Neoplasia

Clinical Findings Associated with Insulin-Secreting Tumors

- Seizures
- Weakness
- Collapse
- Ataxia

Polyphagia
Weight gain
Muscle fasciculations
Posterior weakness (neuropathy)
Lethargy
Nervousness
Unusual behavior

Gastrinoma (Zollinger-Ellison Syndrome)

Clinical Findings

Clinical Signs

Vomiting
Weight loss
Anorexia
Diarrhea
Gastric and duodenal ulceration
Hematochezia
Hematemesis
Melena
Obstipation
Lethargy/depression
Abdominal pain
Esophageal pain and ulceration
Regurgitation
Fever
Polydipsia
Thin body condition
Pallor

Clinicopathologic Findings

Regenerative anemia
Hypoproteinemia
Neutrophilic leukocytosis
Hypoalbuminemia
Hypocalcemia
Mild increases in hepatic enzymes
Hypochloremia
Hypokalemia
Hyponatremia
Metabolic acidosis
Metabolic acidosis (secondary to vomiting)
Hyperglycemia, hypoglycemia (uncommon)

Glucagonoma

Clinical Findings in Dogs

Clinical Signs

Necrolytic migratory erythema (crusting skin rash of elbows, hocks, nose, scrotum, flank, ventral abdomen, distal extremities, and mucocutaneous junctions of mouth, eyes, prepuce and vulva)
Footpad lesions
Glucose intolerance/diabetes mellitus (caused by excess glycogenolysis and gluconeogenesis)
Oral ulcerations
Lethargy
Weight loss
Decreased appetite
Muscle atrophy
Peripheral lymphadenopathy

Clinicopathologic Findings

Hyperglycemia
Nonregenerative anemia
Increased hepatic enzymes
Decreased albumin
Decreased globulin
Decreased blood urea nitrogen (BUN)
Decreased cholesterol
Glucosuria
Abdominal ultrasound lesions

- Increased echogenicity of portal and hepatic vein walls
- Diffuse hyperechogenicity
- Multiple small hypoechoic foci

Hyperadrenocorticism

Clinical Findings

Potential Clinical Signs

Polyuria/polydipsia
Alopecia
Pendulous abdomen
Hepatomegaly
Polyphagia
Muscle weakness
Muscle atrophy
Pyoderma

Comedones
Panting
Pacing/restlessness
Hyperpigmentation
Systemic hypertension
Testicular atrophy
Anestrus
Calcinosis cutis
Facial nerve paralysis
Pulmonary thromboembolism

Potential Clinicopathologic Findings

Urinary tract infection/pyelonephritis
Decreased urine specific gravity
Increased serum alkaline phosphatase (ALP)
Increased alanine aminotransferase (ALT)
Hypercholesterolemia
Hypertriglyceridemia
Hyperglycemia (mild to moderate)
Diabetes mellitus (uncommon)
Increased serum bile acids
Decreased BUN and creatinine (secondary to diuresis)
Hypophosphatemia
Stress leukogram
- Neutrophilia
- Lymphopenia
- Eosinopenia
- Monocytosis

Thrombocytosis
Mild erythrocytosis
Decreased total serum thyroxine (T_4) or free T_4
Urolithiasis

Hyperglycemia

Differential Diagnosis

Diabetes mellitus
Stress (physiologic in cat)
Hyperadrenocorticism
Drug therapy
- Glucocorticoids
- Progestagens
- Megestrol acetate
- Thiazide diuretics

Dextrose-containing fluids
Parenteral nutrition

Postprandial effect (diets containing monosaccharides, disaccharides, propylene glycol)
Exocrine pancreatic neoplasia
Pancreatitis
Renal insufficiency
Acromegaly (cat)
Pheochromocytoma (dog)
Diestrus (bitch)
Head trauma

Hypoadrenocorticism

Potential Clinical Findings

Clinical Signs

Lethargy/depression
Episodic weakness
Vomiting
Anorexia
Waxing and waning illness
Weight loss/failure to gain weight
Bradycardia
Dehydration/hypovolemia
Diarrhea
Polyuria or polydipsia
Collapse
Syncope
Restlessness/shaking/shivering
Regurgitation
Muscle cramping
Gastrointestinal hemorrhage/melena
Abdominal pain

Potential Clinicopathologic Findings

Hyponatremia
Hyperkalemia
Hypochloremia
Decreased sodium/potassium ratio (<24:1)
Azotemia
- Increased blood urea nitrogen (BUN)
- Increased creatinine
- Increased phosphate

Decreased bicarbonate and total CO_2 concentrations
Hypercalcemia
Hypoglycemia
Hypoalbuminemia
Increased hepatic enzymes

Metabolic acidosis
Lymphocytosis
Eosinophilia
Relative neutropenia
Anemia (usually nonregenerative)
Variable urine specific gravity (<1.030)

Hypoglycemia

Differential Diagnosis

Excess Secretion of Insulin or Insulin-Like Factors
- Insulinoma
- Extrapancreatic tumor
- Islet cell hyperplasia

Decreased Glucose Production
- Toy breeds
- Neonates
- Malnutrition
- Pregnancy
- Fasting
- Hypoadrenocorticism
- Hypopituitarism
- Growth hormone deficiency
- Liver disease (portal caval shunt, chronic fibrosis/cirrhosis)
- Glycogen storage diseases

Excess Glucose Consumption
- Sepsis
- Extreme exercise

Drug-Associated Causes
- Insulin
- Oral hypoglycemics
- Many other drugs reported to cause hypoglycemia in humans

Spurious
- Blood cells not promptly separated from serum

Hyponatremia/Hyperkalemia

Differential Diagnosis

Hypoadrenocorticism

Renal or Urinary Tract Disease
- Urethral obstruction
- Acute renal failure
- Chronic oliguric or anuric renal failure

Postobstructive diuresis
Nephrotic syndrome

Severe Gastrointestinal Disease
Parasitic infestation
- Whipworm (trichuriasis)
- Roundworm (ascariasis)
- Hookworm (ancylostomiasis)

Salmonellosis
Viral enteritis
- Parvovirus
- Canine distemper virus

Gastric dilatation/volvulus
Gastrointestinal perforation
Severe malabsorption
Hemorrhagic gastroenteritis
Pancreatic disease

Severe Hepatic Failure
Cirrhosis
Neoplasia

Severe Metabolic or Respiratory Acidosis

Congestive Heart Failure

Massive Release of Potassium into Extracellular Fluid
Crush injury
Aortic thrombosis
Rhabdomyolysis
- Heat stroke
- Exertional

Massive sepsis
Massive hemolysis

Pleural Effusion

Pregnancy

Lymphangiosarcoma

Pseudohyperkalemia
Akitas and related breeds
Severe leukocytosis (>100,000/mm^3)
Severe thrombocytosis (>1 million/mm^3)

Diabetes Mellitus

Primary Polydipsia

Inappropriate Antidiuretic Hormone (ADH) Secretion

Drug Induced
Potassium-sparing diuretics
Nonsteroidal antiinflammatory drugs (NSAIDs)

Angiotensin-converting enzyme (ACE) inhibitors
Potassium-containing fluids

Insulinoma

Differential Diagnosis for Insulin-Secreting Beta-Cell Neoplasia

Excess Insulin or Insulin-Like Factors
- Insulinoma
- Extrapancreatic tumor
- Islet cell hyperplasia

Decreased Glucose Production
- Hypoadrenocorticism
- Hypopituitarism
- Growth hormone deficiency
- Liver disease
- Glycogen storage diseases
- Neonates
- Toy breeds
- Fasting
- Malnutrition
- Pregnancy

Excess Glucose Consumption
- Sepsis
- Extreme exercise

Drug-Associated Causes
- Insulin
- Oral hypoglycemics (sulfonylurea)
- Salicylates (e.g., aspirin)
- Acetaminophen
- β-blockers
- β_2-agonists
- Ethanol
- Monoamine oxidase inhibitors
- Tricyclic antidepressants
- Angiotensin-converting enzyme (ACE) inhibitors
- Antibiotics (e.g., tetracycline)
- Lidocaine overdose
- Lithium

Factitious Hypoglycemia
- Failure to separate blood cells from serum promptly
- Severe polycythemia or leukocytosis when serum separation delayed

Parathyroidism

Hyperparathyroidism, Primary—Clinical Findings

Clinical Signs

- Polyuria/polydipsia
- Weight loss
- Anorexia
- Lethargy, listlessness
- Urinary tract infection (UTI)
- Urolithiasis
- Vomiting
- Constipation
- Mental dullness, obtundation, coma
- Weakness, muscle wasting, shivering

Clinicopathologic Findings

- Hypercalcemia
- Increased ionized calcemia
- Low normal to low serum phosphorus
- Decreased urine specific gravity
- Hematuria
- Pyuria
- Crystalluria
- Bacteriuria

Hypoparathyroidism—Clinical Findings

Clinical Signs

- Seizures
- Facial rubbing, biting at feet
- Splinted abdomen
- Stiff gait
- Intermittent lameness
- Muscle fasciculations, cramping, tremors
- Fever
- Paroxysmal tachyarrhythmias
- Muffled heart sounds
- Weak pulses
- Disorientation

Clinicopathologic Findings

- Hypocalcemia
- Hyperphosphatemia
- Decreased serum parathyroid hormone concentration

Electrocardiographic Findings

- Deep, wide T waves
- Prolonged QT interval
- Bradycardia

Pheochromocytoma

Clinical Findings

Intermittent weakness
Intermittent collapse
Panting
Tachypnea
Seizures
Tachycardia
Lethargy
Inappetence
Cardiac arrhythmias
Restlessness
Exercise intolerance
Weak pulses
Vomiting
Diarrhea
Weight loss
Muscle wasting
Polyuria/polydipsia
Abdominal distension
Rear limb edema
Pale mucous membranes
Abdominal pain
Hemorrhage (epistaxis, surgical incision sites)
Palpable abdominal mass

Pituitary Dwarfism

Clinical Findings

Musculoskeletal Signs

Stunted growth
Delayed growth plate closure
Thin skeleton
Immature facial features
Square, chunky contour as adult
Bone deformities
Delayed dental eruption

Dermatologic Signs

Soft, woolly haircoat
Lack of guard hairs
Alopecia; bilaterally symmetric trunk, neck, and proximal extremities
Hyperpigmentation
Thin, fragile skin

Wrinkles
Scales
Comedones
Papules
Pyoderma
Seborrhea sicca
Retention of secondary hairs

Reproductive Signs

Testicular atrophy
Unilateral or bilateral cryptorchidism
Flaccid penile sheath
Failure to have estrous cycles

Other Signs

Mental dullness
Shrill, puppy-like bark
Signs of secondary hypothyroidism
Signs of secondary adrenal insufficiency

Thyroid Disease

Hyperthyroidism, Feline—Clinical Findings

Clinical Signs

Weight loss/thin body condition
Polyphagia
Hyperactivity
Palpable thyroid nodule (goiter)
Tachycardia
Vomiting
Cardiac murmur
Premature beats
Gallop rhythm
Aggressiveness
Panting
Pacing
Restlessness
Increased nail growth
Alopecia
Polyuria/polydipsia
Diarrhea
Increased fecal volume
Muscle weakness
Congestive heart failure (CHF)
Dyspnea
Ventroflexion of neck

Unkempt coat/alopecia
Tremor
Weakness
Anorexia

Hypothyroidism, Canine—Clinical Findings

Clinical Signs

Lethargy/exercise intolerance
Weight gain
Cold intolerance
Mental dullness
Dermatologic signs
- Alopecia
- Superficial pyoderma
- Seborrhea sicca or oleosa
- Dry, scaly skin
- Changes in haircoat quality and color
- Hyperkeratosis
- Hyperpigmentation
- Comedones
- Hypertrichosis
- Ceruminous otitis
- Myxedema (cutaneous mucinosis)
- Poor wound healing
- Slow regrowth of hair

Reproductive abnormalities
- Male: decreased libido, testicular atrophy, hypospermia
- Female: delayed estrus, silent estrus, failure to cycle, abortion, small litters, uterine inertia, weak or stillborn puppies

Peripheral neuropathies
- Generalized peripheral neuropathies
- Specific peripheral neuropathies (especially cranial nerves, facial, trigeminal, vestibulocochlear)

Cerebral dysfunction (myxedema coma [rare])
Cardiovascular signs
- Sinus bradycardia, weak apex beat, low QRS voltages, inverted T waves, hypercholesterolemia leading to atherosclerosis (rare)

Ocular abnormalities (corneal lipidosis, corneal ulceration, uveitis, secondary glaucoma, lipemia retinalis, retinal detachment, and keratoconjunctivitis sicca reported, but causal relationship not proven)

Clinicopathologic Changes

Nonregenerative anemia
Hypercholesterolemia
Hypertriglyceridemia
Mild increases in hepatic enzymes

SECTION IV

Gastroenterologic Disorders

Chronic Constipation, Feline

Differential Diagnosis

Neuromuscular Dysfunction

- Colonic smooth muscle: idiopathic megacolon, aging
- Spinal cord disease: lumbosacral disease, cauda equina syndrome, sacral spinal cord deformities (Manx cat)
- Hypogastric or pelvic nerve disorders: traumatic injury, malignancy, dysautonomia

Mechanical Obstruction

- Intraluminal: foreign material, neoplasia, rectal diverticula, perineal hernia, anorectal strictures
- Intramural: neoplasia
- Extraluminal: pelvic fractures, neoplasia

Inflammation

- Perianal fistula, proctitis, anal sac abscess, anorectal foreign bodies, perianal bite wounds

Metabolic and Endocrine

- Metabolic: dehydration, hypokalemia, hypercalcemia
- Endocrine: hypothyroidism, obesity, nutritional secondary hyperparathyroidism

Environmental and Behavioral

- Soiled litter box, inactivity, hospitalization, change in environment

Diarrhea

Causes of Diarrhea

Gastrointestinal Disease

- Diffuse gastrointestinal disease (e.g., inflammation or lymphoma)
- Gastric disease (achlorhydria, dumping syndromes)
- Intestinal disease (primary small intestinal disease, primary large intestinal disease, dietary-induced such as food poisoning, gluttony, or sudden change of diet)

Nongastrointestinal Disease

- Pancreatic disease (exocrine pancreatic insufficiency, pancreatitis, pancreatic carcinoma, gastrinoma or Zollinger-Ellison syndrome)
- Liver disease (hepatocellular failure, intrahepatic and extrahepatic cholestasis)
- Endocrine disease (classical hypoadrenocorticism, atypical hypoadrenocorticism, hyperthyroidism, hypothyroidism)
- Renal disease (uremia, nephrotic syndrome)
- Polysystemic infection (e.g., distemper, leptospirosis, infectious canine hepatitis in dogs, FIP, FeLV, FIV in cats)
- Miscellaneous (toxemias such as pyometra and peritonitis, congestive heart failure, autoimmune disease, metastatic neoplasia, various toxins and drugs)

Classification of Diarrhea

Mechanistic

- Secretory
- Osmotic
- Permeability (exudative)
- Dysmotility
- Mixed

Temporal

- Acute
- Chronic

Anatomic

- Extraintestinal
- Small intestinal
- Large intestinal
- Diffuse

Pathophysiologic
- Biochemical
- Allergic
- Inflammatory
- Neoplastic

Etiologic
- Bacteria
- Dietary
- Fungal
- Idiopathic
- Parasitic
- Viral

Causal
- Exocrine pancreatic insufficiency, salmonellosis, lymphoma, other

Clinical
- Acute, nonfatal, mild, self-limiting
- Acute, severe potentially fatal
- Acute systemic disease
- Chronic
- Chronic protein-losing

Dental and Oral Cavity Diseases

Differential Diagnosis

Trauma

Fractures
- Crown
- Root
- Mandible
- Maxillary

Avulsion
Pulp injury
Temporomandibular luxation

Caries

Feline Dental Resorptive Lesions

Periodontal Disease

Gingivitis
Gingival recession
Bone loss, osteomyelitis
Tooth loss

Tooth Root Abscess

Oronasal Fistula

Stomatitis (Faucitis, Glossitis, Pharyngitis)

Feline immunodeficiency virus, feline leukemia virus, feline syncytium-forming virus
Feline calicivirus, feline herpesvirus, feline infectious peritonitis
Candidiasis
Uremia
Trauma (foreign objects, caustic agents, electric cord bite)
Autoimmune disease (pemphigus, lupus, idiopathic vasculitis, toxic epidermal necrolysis)
Feline idiopathic gingivitis/pharyngitis

Neoplasia

Malignant

Fibrosarcoma
Squamous cell carcinoma
Melanoma
Salivary gland neoplasms

Benign

Epulis
- Fibromatous
- Acanthomatous
- Ossifying
- Papilloma
- Fibroma
- Lipoma
- Chondroma
- Osteoma
- Hemangioma
- Hemangiopericytoma
- Histiocytoma

Eosinophilic Granuloma Complex

Linear granuloma
Eosinophilic ulcer (usually on maxillary lips)

Sialocele

Diseases of the Tongue

Differential Diagnosis

Trauma

- Mechanical injury (sharp objects)
- Chemical injury
- Electric shock (electric cord)

- Foreign body (plant material, porcupine quill, linear foreign bodies)
- Sublingual hyperplastic tissue (gum chewer's disease)

Viral
- Calicivirus
- Herpes virus
- Papillomavirus

Neoplasia
- Malignant melanoma
- Squamous cell carcinoma
- Benign tumors (lipoma, plasma cell tumor, granular cell tumors, fibroma)

Metabolic Disease (Uremia)

Sublingual Mucocele (Ranula)

Immune Mediated
- Mucous membrane pemphigoid
- Pemphigus vulgaris
- Bullous pemphigoid
- Systemic lupus erythematosus
- Autoimmune vasculopathies (idiopathic, infectious, food allergies, drug reaction, neoplasia)

Eosinophilic granulomas

Contact Mucosal Ulceration from Calculus Contact

Calcinosis Circumscripta

Salivary Gland Disease

Differential Diagnosis

Salivary Neoplasia (more common in cats than dogs)
Adenocarcinoma
Squamous cell carcinoma
Undifferentiated sarcoma
Mucoepidermoid tumor
Malignant mixed tumor
Sarcoma
Acinic cell carcinoma
Adenoid cystic carcinoma

Salivary Mucocele
Sublingual gland most commonly

Sialoadenitis

Sialadenosis

Esophageal Disease

Differential Diagnosis

Congenital

Obstruction

Persistent right aortic arch
Persistent right or left subclavian artery
Other vascular ring anomaly

Idiopathic

Acquired

Obstruction

Foreign body
Cicatrix/stricture
Neoplasia
- Carcinoma
- *Spirocerca lupi*–induced sarcoma
- Leiomyoma of lower esophageal sphincter
- Extraesophageal neoplasia
  - Thyroid carcinoma
  - Pulmonary carcinoma
  - Mediastinal lymphosarcoma

Achalasia of lower esophageal sphincter (rare)
Gastroesophageal intussusception (rare)

Weakness

Myasthenia (generalized or localized)
Hypoadrenocorticism
Esophagitis
Persistent vomiting
Hiatal hernia
Gastroesophageal reflux/anesthesia-associated reflux
Caustic ingestion (doxycycline, disinfectants, chemicals, etc.)
Foreign body
Excess gastric acidity (gastrinoma, mast cell tumor)
Fungal organisms (e.g., pythiosis)

Spirocerca lupi Infection

Myopathies/Neuropathies

Hypothyroidism
Systemic lupus erythematosus (SLE)
Others

Miscellaneous Causes

Lead poisoning
Chagas disease

Canine distemper
Dermatomyositis (principally in Collies)
Dysautonomia
Tetanus

Idiopathic

Stomach Disorders

Differential Diagnosis

Gastritis

Acute Gastritis

Dietary indiscretion
Dietary intolerance or allergy
Foreign body
Drugs and toxins (nonsteroidal antiinflammatory drugs [NSAIDs], corticosteroids, antibiotics, plants, cleaners, bleach, heavy metals)
Systemic disease (uremia, hepatic disease, hypoadrenocorticism)
Parasites (*Ollulanus* spp., *Physaloptera* spp.)
Bacterial (bacterial toxins, *Helicobacter* spp.)

Hemorrhagic Gastroenteritis

Chronic Gastritis

Lymphocytic/plasmacytic gastritis (inflammatory reaction to a variety of antigens such as *Helicobacter* spp. or *Physaloptera rara*)
Eosinophilic gastritis (allergic reactions to food antigens)
Granulomatous gastritis (e.g., *Ollulanus tricuspis*)
Atrophic gastritis

Gastric Outflow Obstruction/Gastric Stasis

Benign muscular pyloric hypertrophy (pyloric stenosis)
Gastric antral mucosal hypertrophy
Foreign body
Idiopathic gastric hypomotility
Bilious vomiting syndrome

Gastric Ulceration/Erosion

Iatrogenic

NSAIDs
Corticosteroids
NSAID/corticosteroid combinations

Foreign Body

***Helicobacter* spp.**

Stress Ulceration

Hypovolemic shock
Septic shock
After gastric dilatation/volvulus
- Neurogenic shock

Hyperacidity
- Mast cell tumor
- Gastrinoma (rare)

Other causes
- Hepatic disease
- Renal disease
- Hypoadrenocorticism
- Inflammatory disease

Infiltrative Disease

Neoplasia
Inflammatory bowel disease
Pythiosis (young dogs, southeastern United States)

Gastric Dilatation/Volvulus

Causes of Acute Abdomen

Gastrointestinal (GI) Causes

Acute pancreatitis
Gastroenteritis (parvoviral, bacterial, toxic, hemorrhagic gastroenteritis, etc.)
Gastric dilatation/volvulus
Intestinal obstruction/intussusception/volvulus
Colitis
Obstipation
Necrosis, rupture, ulceration, or perforation of GI tract
Surgical wound dehiscence
Mesenteric torsion
Duodenocolic ligament entrapment
Pancreatic abscess
Pancreatic neoplasia

Hepatobiliary Causes

Acute hepatitis/cholangiohepatitis
Biliary obstruction
Necrotizing cholecystitis
Hepatic abscess
Bile peritonitis

Liver lobe torsion
Hepatic trauma/rupture
Hepatobiliary neoplasia

Urogenital Causes

Urethral or ureteral obstruction/rupture
Pyelonephritis
Renal neoplasia
Acute nephrosis/nephritis
Cystic, renal, ureteral, or urethral calculi
Prostatitis/prostatic abscess/prostatic cyst/prostatic neoplasia
Dystocia
Pyometra/uterine rupture
Acute metritis
Renal abscess
Testicular torsion
Ovarian cyst, ovarian neoplasia
Uterine torsion
Uroabdomen
Vaginal rupture

Other Causes

Penetrating wound, crush injury
Peritonitis (septic, chemical, urine, bile)
Mesenteric traction (large masses)/lymphadenitis/lymphadenopathy/volvulus/avulsion/artery thrombosis
Hemoabdomen (parenchymatous organ rupture)
Neoplasia
Splenic torsion/abscess/mass/rupture
Strangulated hernia
Adhesions with organ entrapment
Pansteatitis
Retroperitoneal hemorrhage
Evisceration
Surgical contamination

Small Intestinal Disease

Clinical Findings

Diarrhea
Vomiting
Inappetence/anorexia
Malabsorption
Protein-losing enteropathy
Weight loss
Dehydration

Hematemesis
Melena
Polyphagia
Coprophagia
Abdominal distension
Abdominal pain
Borborygmus/flatulence
Ascites
Edema
Shock
Halitosis
Polydipsia
Ileus

Differential Diagnosis

Acute Diarrhea

Acute enteritis
Dietary indiscretion
Enterotoxemia

Infectious Diarrhea

Canine parvoviral enteritis
Clostridial disease
Feline parvoviral enteritis (panleukopenia)
Canine coronaviral enteritis
Feline coronaviral enteritis
Feline leukemia virus–associated panleukopenia
Feline immunodeficiency virus–associated diarrhea
Salmon poisoning *(Neorickettsia helminthoeca)*
Campylobacteriosis
Salmonellosis
Histoplasmosis
Miscellaneous *bacteria (Yersinia enterocolitica, Aeromonas hydrophila, Plesiomonas shigelloides)*
Protothecosis (algae)

Alimentary Tract Parasites

Roundworms (*Toxocara* spp.)
Hookworms (*Ancylostoma, Uncinaria* spp.)
Tapeworms (*Dipylidium caninum, Taenia* spp., *Mesocestoides* spp.)
Strongyloides stercoralis (in puppies)
Coccidiosis
Cryptosporidia
Giardiasis
Trichomoniasis
Heterobilharzia

Maldigestive Disease
- Exocrine pancreatic insufficiency

Malabsorptive Disease
- Dietary-responsive disease (allergy, intolerance)
- Inflammatory bowel disease (lymphocytic/plasmacytic enteritis canine eosinophilic gastroenteritis)
- Feline eosinophilic enteritis/hypereosinophilic syndrome
- Granulomatous enteritis
- Immunoproliferative enteropathy in Basenjis
- Enteropathy in Shar-Peis
- Antibiotic-responsive enteropathy

Protein-Losing Enteropathy
- Intestinal lymphangiectasia
- Protein-losing enteropathy in Soft-Coated Wheaten Terriers

Irritable Bowel Syndrome

Intestinal Obstruction
- Simple intestinal obstruction
- Incarcerated intestinal obstruction
- Mesenteric torsion/volvulus
- Linear foreign object

Intussusception
- Ileocolic
- Jejunojejunal

Short-Bowel Syndrome

Neoplasia
- Alimentary lymphoma
- Intestinal adenocarcinoma
- Intestinal leiomyoma/leiomyosarcoma

Breed Susceptibilities, Dogs

Basenji: lymphocytic/plasmacytic enteritis (immunoproliferative disease)
Beagle: cobalamin deficiency
Border Collie: cobalamin deficiency
German Shepherd: idiopathic antibiotic-responsive small intestinal disease, inflammatory bowel disease (lymphoplasmacytic, eosinophilic)
Giant Schnauzer: defective cobalamin absorption
Irish Setter: gluten-sensitive enteropathy

Lundehund: lymphangiectasia
Retrievers: dietary allergy
Rottweiler: increased susceptibility to parvoviral enteritis
Soft-Coated Wheaten Terrier: protein-losing enteropathy/nephropathy
Shar-Pei: lymphocytic/plasmacytic enteritis, cobalamin deficiency
Yorkshire Terrier: lymphangiectasia
Toy breeds: hemorrhagic gastroenteritis

Large Intestinal Disease

Differential Diagnosis

Inflammation of Large Intestine

Acute colitis/proctitis
Chronic colitis
- Lymphocytic/plasmacytic colitis
- Eosinophilic enterocolitis
- Chronic ulcerative colitis
- Histiocytic ulcerative colitis (Boxers)

Irritable bowel syndrome

Dietary Intolerance or Food Allergy

Parasites

Whipworms (*Trichuris* spp.)
Tritrichomonas spp. (cats)
Giardiasis
Hookworms (*Ancylostoma* spp.)
Heterobilharzia americanum

Bacterial Colitis

Clostridial colitis
Campylobacter colitis
Escherichia coli
Salmonell a spp.
Brachispira pilosicoli

Fungal Colitis

Histoplasmosis
Pythiosis

Viral Colitis

Feline leukemia virus (FeLV)
Infections secondary to FeLV and feline immunodeficiency virus (FIV)

Algae (*Prototheca* spp.)

Cecocolic Intussusception

Rectal Prolapse

Neoplasms of Large Intestine
- Adenocarcinoma
- Lymphoma
- Rectal polyps

Constipation
- Pelvic canal obstruction caused by malaligned healing of pelvic fractures
- Benign rectal stricture
- Dietary indiscretion leading to constipation
- Idiopathic megacolon

Ileus

Causes

Physical
- Intestinal obstruction (foreign body, intussusception, neoplasia, granuloma, torsion, volvulus, incarceration in hernia)
- Overdistension by aerophagia

Metabolic
- Uremia
- Diabetes mellitus
- Hypokalemia
- Endotoxemia

Inflammatory
- Parvovirus
- Peritonitis
- Other inflammatory causes

Functional
- Abdominal surgery
- Peritonitis
- Pancreatitis
- Ischemia

Neuromuscular
- Anticholinergic drugs
- Spinal cord injury
- Visceral myopathies/neuropathy
- Dysautonomia

Malabsorptive Diseases

Causes

Food intolerance or allergy
Parasitism
- Giardiasis

Bacterial overgrowth
Inflammatory bowel disease
- Lymphocytic/plasmacytic enteritis
- Eosinophilic enteritis
- Idiopathic villous atrophy
- Purulent enteritis

Gastrointestinal lymphoma
Lymphangiectasia
Obstruction caused by neoplasia, infection, or inflammation
Portal hypertension
Pythiosis
Exocrine pancreatic insufficiency
Cholestatic liver disease/biliary obstruction
Brush border enzyme deficiencies
Brush border transport protein deficiencies
Hyperthyroidism
Gastric hypersecretion

Perianal Disease

Differential Diagnosis

Perineal hernia
Perianal fistulae
Anal sacculitis
Anal sac impaction
Abscessed anal sac
Anal sac (apocrine gland) adenocarcinoma
Perianal gland tumors
- Adenoma (common)
- Adenosarcoma (rare)

Protein-Losing Enteropathy

Differential Diagnosis

Gastrointestinal Hemorrhage
Hemorrhagic gastroenteritis
Ulceration
Neoplasia

Endoparasites
- *Giardia* spp.
- *Ancylostoma* spp.
- Coccidia
- Others

Inflammation
- Lymphocytic/plasmacytic
- Eosinophilic
- Granulomatous

Infection
- Parvovirus
- Salmonellosis
- Histoplasmosis
- Phycomycosis

Structural
- Intussusception

Neoplasia
- Lymphosarcoma

Lymphangiectasia
- Primary lymphatic disorder
- Venous hypertension (e.g., right heart failure)
- Hepatic cirrhosis

Fecal Incontinence

Causes

Nonneurologic Disease

Colorectal Disease
- Inflammatory bowel disease
- Neoplasia
- Constipation

Anorectal Disease
- Perianal fistula
- Neoplasia
- Surgery (anal sacculectomy, perianal herniorrhaphy, rectal resection and anastomosis)

Miscellaneous
- Decreased mentation
- Old age
- Severe diarrhea
- Irritable bowel disease

Neurologic Disease

Sacral Spinal Cord Disease

- Discospondylitis
- Neoplasia
- Degenerative myelopathy
- Congenital vertebral malformation
- Sacrococcygeal hypoplasia of Manx cats
- Sacral fracture
- Sacrococcygeal subluxation
- Lumbosacral instability
- Lumbrosacral nerve root compression
- Meningomyelocele
- Viral meningomyelitis
- Cauda equina syndrome
- Vertebral fracture

Peripheral Neuropathy

- Trauma
- Penetrating wounds
- Repair of perineal hernia
- Perineal urethrostomy
- Hypothyroidism?
- Diabetes mellitus?
- Dysautonomia

Central Nervous System

- Infectious (distemper, feline infectious peritonitis)
- Neoplasia
- Vascular compromise

SECTION V

Hematologic Disorders

Anemia

Hemolytic Anemia

Causes/Triggers of Immune-Mediated Hemolytic Anemia

Infection

Viral

Feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline peritonitis virus (FIP), chronic upper respiratory or gastrointestinal (GI) disease

Bacterial

Leptospirosis, *Mycoplasma haemophilus* infection, salmonellosis, acute and chronic infections (e.g., abscess, pyometra, discospondylitis)

Parasitic

Babesiosis, anaplasmosis, leishmaniasis, dirofilariasis, ehrlichiosis, *Ancylostoma caninum, Trichuris vulpis* infection, bartonellosis

Immune Disorders

Systemic lupus erythematosus (SLE)
Hypothyroidism
Primary and secondary immunodeficiencies

Drugs/Toxins

Vaccines
Sulfonamides
Methimazole
Procainamide
Cephalosporins
Penicillins
Propylthiouracil
Carprofen
Levamisole

Griseofulvin
Bee-sting envenomation

Oxidants

Acetaminophen
Phenothiazines
Vitamin K
Methylene blue
Methionine
Propylene glycol

Inflammation

Pancreatitis
Prostatitis/cystitis

Neoplasia

Leukemias
Lymphoma
Multiple myeloma
Mast cell tumor
Splenic hemangioma
Solid tumors

Genetic Predisposition

American Cocker Spaniel (most common breed), English Springer Spaniel, Old English Sheepdog, Irish Setter, Poodle, Dachshund, Alaskan Malamute, Schnauzer

Differentiating Blood Loss from Hemolytic Anemia

Blood Loss

Serum or plasma protein concentration normal to low
Clinical evidence of hemorrhage
No icterus, hemoglobinemia, spherocytosis, hemosiderinuria, autoagglutination, splenomegaly, or red blood cell (RBC) changes
Negative direct Coombs test

Hemolysis

Serum or plasma protein concentration normal to high
Rarely clinical evidence of hemorrhage
Icterus common
Hemoglobinuria/hemoglobinemia
Spherocytosis
Hemosiderinuria
Autoagglutination sometimes seen
Direct Coombs test usually positive
Splenomegaly
RBC changes numerous

Nonregenerative Anemia

Differential Diagnosis

Anemia of Chronic Disease

Erythropoietin-Related Conditions
- Renal disease
- Hypothyroidism
- Hypoadrenocorticism
- Panhypopituitarism
- Growth hormone deficiency
- Reduced oxygen requirement
- Increased oxygen release

Iron Deficiency Anemia
- Chronic inflammation
- Chronic hemorrhage
- Dietary iron deficiency

Marrow Disorders

Toxic Red Cell Aplasia
- Estrogen related
- Phenylbutazone related
- Other drugs

Hyperestrogenism (Iatrogenic, Neoplastic)

Infection
- Feline leukemia virus (FeLV)
- Feline immunodeficiency virus (FIV)
- Parvovirus
- Ehrlichiosis
- Babesiosis
- *Mycoplasma haemofelis*
- Endotoxemia

Immunotherapy

Myelofibrosis
- Feline leukemia virus (FeLV) infection
- Pyruvate kinase deficiency anemia
- Idiopathic

Myelophthisic Disease
- Acute leukemias
- Chronic leukemias
- Multiple myeloma
- Lymphoma
- Systemic mast cell disease Malignant histiocytosis
- Metastatic carcinoma
- Histoplasmosis

Myelodysplasia
- Idiopathic
- FeLV/FIV
- Preleukemic syndrome

Pure Red Cell Aplasia

Ineffective Erythropoiesis

Macrocytic (rare)
- Intrinsic marrow disease
- Vitamin B_{12} deficiency
- Folic acid deficiency

Normocytic
- Myelofibrosis
- Intrinsic erythroid disease

Microcytic
- Iron deficiency
- Globin or porphyrin deficiency

Time Related
- Hemolysis or hemorrhage (during the first 3-5 days)

Diagnosis

Nonregenerative Anemias without Other Cytopenias

Examine bone marrow.

Severe Erythroid Hypoplasia
- Pure red cell aplasia

Normal to Mild Erythroid Hypoplasia
- Inflammatory disease
- Renal disease
- Neoplasia
- Hepatic disease
- Hypothyroidism
- Hypoadrenocorticism

Hypercellular Bone Marrow
- Less than 30% blast forms: consider myelodysplastic syndrome
- Greater than 30% blast forms: consider hemopoietic neoplasia

Nonregenerative Anemias with Leukopenia and/or Thrombocytopenia

Examine bone marrow.

Panhypoplasia
- Aplastic anemia

Disease Determined by Core Biopsy
Myelonecrosis
Myelofibrosis

Hypercellular Bone Marrow
Less than 30% blast forms: myelodysplastic syndrome
More than 30% blast forms: hemopoietic neoplasia

Regenerative Anemia

Differential Diagnosis

Hemolysis

Immune mediated
- Intravascular
- Extravascular

Blood Loss Anemia

Trauma
Coagulopathy
- Clotting factor deficiency
- Disseminated intravascular coagulation (DIC)
- Platelet disorders
- Anticoagulant rodenticides

Endoparasites
GI blood loss
Severe ectoparasites (fleas)

Oxidative Injury (Heinz Body)

Onion ingestion
Acetaminophen (cats)
Zinc ingestion (pennies minted after 1982, zinc oxide ointment, zinc-plated bolts and screws)
Benzocaine ingestion (dogs)
D-L Methionine (cats)
Phenolic compounds (mothballs)
Phenazopyridine (cats)

Erythrocytic Parasites

Haemobartonella spp.
Babesia spp.
Cytauxzoon spp.

Fragmentation (Microangiopathic)

Disseminated intravascular coagulation (DIC)
Heartworm disease
Hemangiosarcoma
Vasculitis
Hemolytic-uremic syndrome
Diabetes mellitus

Other

Copper toxicity
Neonatal isoerythrolysis
Hereditary nonspherocytic hemolytic anemia
Pyruvate kinase deficiency
Feline porphyria
Hemolysis in Abyssinian and Somali cats

Coagulopathies, Inherited and Acquired

Differential Diagnosis

Inherited Clotting Factor Deficiencies

Hemophilia A (factor VIII deficiency)
Hemophilia B (factor IX deficiency)
Factor XII deficiency (Hageman trait) (Miniature and Standard Poodle, Shar-Pei, German Shorthair Pointer, cats)
Vitamin K–dependent factor deficiency: factors II, VII, IX, X (Devon Rex cats)
Factor I: hypofibrinogenemia or dysfibrinogenemia (St. Bernard, Borzoi)
Factor II: hypoprothrombinemia (Boxer, Otterhound, English Cocker Spaniel)
Factor VII: hypoproconvertinemia (Beagle, Malamute, Boxer, Bulldog, Miniature Schnauzer)
Factor X deficiency (Cocker Spaniel, Parson Russell Terrier)
Hemophilia C (factor XI deficiency: English Springer Spaniel, Great Pyrenees, Kerry Blue Terrier)
Prekallikrein deficiency (Fletcher factor)

Acquired Clotting Factor Deficiency

Liver disease
- Decreased clotting factor production
- Qualitative disorders

Cholestasis
Vitamin K antagonists
Autoimmune disease (lupus anticoagulant)
Disseminated intravascular coagulation (DIC)
Neoplasia

Clinical Manifestations of Primary and Secondary Hemostatic Defects

Primary Hemostatic Defects

Thrombocytopenia and diseases that cause platelet dysfunction such as uremia, von Willebrand disease, monoclonal gammopathies,

and vector-borne diseases)—typically see manifestations of superficial bleeding

- Petechiae, ecchymoses
- Bleeding from mucosal surfaces (e.g., bleeding from gingiva, melena, hematochezia, epistaxis, hematuria)
- Bleeding in skin
- Hematomas rare
- Prolonged bleeding immediately after venipuncture

Secondary Hemostatic Defects

Clotting factor deficiencies, rodenticide poisoning, liver disease—typically see manifestations of deep bleeding

- Petechiae, ecchymoses rare
- Hematomas common
- Bleeding into body cavities, joints, muscles
- Delayed bleeding after venipuncture

Expected Hemostatic Test Results in Selected Diseases

- Thrombocytopenia—increased buccal mucosal bleeding time (BMBT), decreased platelet count (PLT), normal activated partial thromboplastin time (APTT), normal prothrombin time (PT), normal fibrin degradation products (FDP)
- Platelet dysfunction (e.g., aspirin treatment)—increased BMBT, normal PLT, increased APTT, normal, PT, normal FDP
- Intrinsic pathway defect (e.g., hemophilia A or B)—normal BMBT, normal PLT, increased APTT, normal PT, normal FDP
- Factor VII deficiency—normal BMBT, normal PLT, normal APTT, increased PT, normal, FDP
- Multiple factor defects (e.g., vitamin K antagonism)—normal BMBT, normal PLT, increased APTT, increased PT, normal FDP
- Common pathway defect (e.g., factor X deficiency)—normal BMBT, normal PLT, increased APTT, increased PT, normal FDP
- Disseminated intravascular coagulation (DIC) —increased BMBT, decreased PLT, increased APTT, increased PT, increased FDP
- von Willebrand disease—increased BMBT, normal PLT, normal APTT, normal PT, normal FDP

Leukocyte Disorders

Differential Diagnosis

Pelger-Huët anomaly (many breeds of dogs and cats)
- Neutrophil function not altered

Chédiak-Higashi syndrome (blue smoke-colored Persian cats)

Canine leukocyte adhesion deficiency: fatal defect (Irish Setter and Irish Setter crosses)

Cyclic hemopoiesis (cyclic neutropenia): fatal defect (gray Collies)

Birman cat neutrophil granulation anomaly: neutrophil function not altered

Hypereosinophilic syndrome (cats): may eventually be fatal

Severe combined immunodeficiency of Parson Russell Terriers: fatal defect

Canine X-linked severe combined immunodeficiency: fatal defect (many breeds)

Defective neutrophil function in Doberman Pinscher: need frequent antimicrobial therapy

Immunodeficiency of Shar-Peis

Immunodeficiency of Weimaraners

Lysosomal storage diseases (many types described, all rare, many breeds)

Platelet Dysfunction

Differential Diagnosis

Acquired Platelet Dysfunction

Drugs

Prostaglandin inhibitors (NSAIDs)
Vaccines
Antibiotics
Antifungals
Phenothiazines
Aminophylline
Diltiazem
Isoproterenol

Secondary to Disease

Renal disease
Liver disease
Myeloproliferative disorders

Systemic lupus erythematosus (SLE)
Dysproteinemias

Hereditary
von Willebrand disease (many breeds)
Canine thrombopathia (Basset Hound, Foxhound, Spitz)
Canine thrombasthenic thrombopathia (Otterhound, Great Pyrenees)
Collagen deficiency diseases/Ehler-Danlos syndrome (many breeds)

Splenitis/Splenomegaly

Differential Diagnosis for Splenomegaly

Splenic Mass (Asymmetric Splenomegaly)
Nodular hyperplasia (lymphoid, fibrohistiocytic)
Hematoma
Neoplasia
- Hemangiosarcoma
- Hemangioma
- Leiomyosarcoma
- Fibrosarcoma
- Histiocytic sarcoma
- Leiomyoma
- Myelolipoma
- Metastatic disease

Abscess
Extramedullary hematopoiesis
Granuloma

Uniform Splenomegaly

Congestion
Drugs
Portal hypertension
Right-sided heart failure
Splenic torsion

Hyperplasia
Chronic infection
Inflammatory bowel disease
Systemic lupus erythematosus (SLE)
Polycythemia vera

Extramedullary Hematopoiesis
Chronic anemia
Immune-mediated hemolytic anemia
Immune-mediated thrombocytopenia

Neoplasia
- Lymphoma
- Systemic mastocytosis
- Primary mast cell tumor
- Metastatic neoplasia
- Multiple myeloma
- Acute and chronic leukemias
- Malignant histiocytosis
- Polycythemia vera

Nonneoplastic Infiltrative Disease
- Amyloidosis
- Hypereosinophilic syndrome (cats)

Inflammation
- Suppurative
- Sepsis
- Bacterial endocarditis
- Infectious canine hepatitis
- Foreign body
- Penetrating wounds
- Toxoplasmosis

Granulomatous
- Cryptococcosis
- Histoplasmosis
- Mycobacteriosis
- Leishmaniasis

Pyogranulomatous
- Feline infectious peritonitis (FIP)
- Blastomycosis
- Sporotrichosis

Eosinophilic
- Eosinophilic gastroenteritis
- Hypereosinophilic syndrome
- Neoplasia

Lymphoplasmacytic
- Ehrlichiosis
- Hemotropic mycoplasmosis
- Lymphoplasmacytic enteritis
- Pyometra
- Brucellosis
- Anaplasmosis

Necrotic Tissue
- Torsion
- Necrotic center of neoplasms

Infectious canine hepatitis
Anaerobic infection
Systemic calicivirosis
Tularemia
Salmonellosis

Infectious Causes

Viral

Feline leukemia virus (FeLV)
Feline immunodeficiency virus (FIV)
Feline infectious peritonitis (FIP)
Infectious canine hepatitis

Bacterial

Canine brucellosis
Mycoplasmosis
Borreliosis
Plague
Tularemia
Streptococcosis
Staphylococcosis
Salmonellosis
Francisella infection
Endotoxemia

Fungal

Cryptococcosis
Histoplasmosis
Blastomycosis

Rickettsial

Ehrlichiosis
Rocky Mountain spotted fever
Q fever *(Coxiella burnetii)*
Mycoplasma haemofelis

Protozoal

Toxoplasmosis
Cytauxzoonosis (cat)
Babesiosis (*Babesia canis* and *B. gibsoni*)
Leishmaniasis (dog)

Thrombocytopenia

Differential Diagnosis

Increased Platelet Destruction/Sequestration/Utilization

Immune-mediated thrombocytopenia
Drug-induced thrombocytopenia

Infectious (*Anaplasma* spp., *Bartonella* spp., sepsis)
Microangiopathy
Disseminated intravascular coagulation
Neoplasia (immune-mediated, microangiography)
Live viral vaccine–induced thrombocytopenia
Hemolytic uremic syndrome/thrombotic thrombocytopenic purpura
Vasculitis
Splenomegaly
Splenic torsion
Endotoxemia
Acute hepatic necrosis
Hemorrhage

Decreased Platelet Production

Drug-induced megakaryocytic hypoplasia (estrogen, phenylbutazone, melphalan, lomustine, β-lactams)
Myelophthisis
Idiopathic bone marrow aplasia
Retroviral infection (FeLV/FIV)
Immune-mediated megakaryocytic hypoplasia
Cyclic thrombocytopenia
Idiopathic bone marrow aplasia
Ehrlichiosis

SECTION VI

Immunologic and Immune-Mediated Disorders

Autoimmune Skin Diseases

Differential Diagnosis

Generalized Pustular/Crusting Dermatosis

- Pemphigus foliaceus (PF) (nose, ear pinna, and footpad typically affected)
- Superficial pustular drug reactions (nasal and footpad lesions may be absent)
- Others: rare presentation—systemic lupus erythematosus (SLE), sterile eosinophilic pustulosis, linear immunoglobulin A (IgA) pustular dermatosis, subcorneal pustular dermatosis

Focal Pustular/Crusting Dermatosis

- Face, footpads: PF
- Face and ears only: PF (early), pemphigus erythematosus (PE), drug eruptions, lupus erythematosus
- Nasal only: discoid lupus erythematosus (DLE), PF (early), PE

Mucocutaneous and Mucosal Ulcerations

- Pemphigus vulgaris (may also have oral lesions)
- Mucous membrane bullous pemphigoid
- Epidermolysis bullosa acquisita
- Erythema multiforme (target lesions, cutaneous lesions)
- Bullous SLE
- Drug reactions
- Linear IgA bullous dermatosis, toxic epidermal necrolysis (rare)

Nonmucosal Ulcerations (Axillae, Inguinae, Pinnae, Other Haired Areas)

- Bullous pemphigoid

Epidermolysis bullosa acquisita
Linear IgA bullous dermatosis
Bullous SLE
Canine vesicular cutaneous lupus erythematosus (idiopathic ulcerative dermatosis of Collies, Shetland Sheepdogs)
Erythema multiforme (EM)
Toxic epidermal necrolysis
Drug eruptions
Pemphigus vulgaris

Depigmenting Skin Diseases
Nasal only: DLE, vitiligo-like syndrome, uveodermatologic syndrome, early PF or PE
Nose, footpad, lip, eyelid, mucocutaneous area: uveodermatologic syndrome (uveitis also)
Haircoat or skin: idiopathic leukotrichia or leukoderma

Miscellaneous
Focal alopecia: alopecia areata, rabies vaccine, focal vasculitis
Widespread noninflammatory alopecia: alopecia areata, pseudopelade
Erythematous target lesions: erythema multiforme
Nodular ulcerative lesions: nodular panniculitis
Purpura, hemorrhage, punched-out lesions
Ear margin necrosis, dependent edema: vasculitis, proliferative necrotizing otitis of kittens, cryoglobulinemia and cryofibrinogenemia, proliferative thrombovascular necrosis of the pinnae

Immune-Mediated Disease

Laboratory Diagnosis

Direct Coombs Test
Immune-mediated hemolytic anemia
Hemolytic anemia in systemic lupus erythematosus (SLE)

Antiplatelet Antibodies
Immune-mediated thrombocytopenia

Antineutrophil Antibodies
Immune-mediated neutropenia

Thyroxin and Thyroglobulin Autoantibodies
Hypothyroidism

Acetylcholine Receptor Autoantibodies
Myasthenia gravis

2M Myofiber Autoantibodies
Masticatory muscle myositis

Antinuclear Antibody
SLE
Chronic antigenic stimulation

Rheumatoid Factor
Rheumatoid arthritis (RA)

Direct Immunofluorescence
Antibody-complement deposition

Differential Diagnosis for Immune-Mediated Arthritis

Erosive Immune-Mediated Arthritides
RA (dog, rarely in cat)
Periosteal proliferative polyarthritis (cat, rarely in dog)

Nonerosive Immune-Mediated Arthritides
Idiopathic polyarthritis
- **Type I:** uncomplicated idiopathic arthritis (most common)
- **Type II:** idiopathic arthritis associated with infection remote from joints—respiratory tract, tonsils, conjunctiva (chlamydia in cats), urinary tract, uterus, skin, oral cavity
- **Type III:** idiopathic arthritis associated with gastroenteritis
- **Type IV:** idiopathic arthritis associated with malignant neoplasia—squamous cell carcinoma, heart base tumor, leiomyoma, mammary carcinoma, myeloproliferative disease (cats)

SLE
Drug-induced polyarthritis
- Sulfas, lincomycin, erythromycin, cephalosporins, penicillins, trimethoprim-sulfa (especially Doberman Pinscher)

Vaccination reaction
Polyarthritis/polymyositis syndrome
Polyarthritis/meningitis syndrome
Familial renal amyloidosis in Chinese Shar-Peis
Polyarthritis in adolescent Akitas
Polyarthritis nodosa (inflammatory condition of small arteries—histopathologic diagnosis)

Immune System Components

Function

Humoral immunity

B Lymphocytes and Plasma Cells

Production of immunoglobulins

Cellular Immunity

T Lymphocytes

Production of lymphokines

Helper T cells

- Stimulate immune reactivity

Suppressor T cells

- Suppress immune reactivity

Antibody-dependent cell-mediated cytotoxicity

Natural killer cells

- Direct cytotoxicity

Phagocytic Cells

Mononuclear Phagocytic Cells

Antigen presentation

Phagocytosis of particles

Neutrophils and Eosinophils

Phagocytosis of particles

Antibody-dependent cell-mediated cytotoxicity

Mechanisms of Immunopathologic Injury

Type I (immediate)

- Humoral immune system (T-helper cells and B cells), IgE, mast cells, inflammatory mediators)
- Skin, respiratory tract, GI tract commonly affected
- Examples include acute anaphylactic reaction, atopy, allergic bronchitis, feline asthma

Type II (cytotoxic)

- Humoral immune system (IgG and IgM)
- Hematologic systems, neuromuscular junctions, and skin commonly affected
- Examples include immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, myasthenia gravis, pemphigus foliaceous

Type III (immune complex)
- Soluble immune complexes
- Kidney, joints, and skin commonly affected
- Examples include glomerulonephritis, systemic lupus erythematosus, rheumatoid arthritis

Type IV (delayed type)
- Sensitized T lymphocytes, cytokines, neutrophils, and macrophages
- Endocrine glands, muscle commonly affected
- Examples include lymphocytic thyroiditis, myositis

Organ Systems Affected by Autoimmune Disorders in the Dog and Cat

Differential Diagnosis

Hematologic
- Immune-mediated hemolytic anemia
- Pure red cell aplasia
- Immune-mediated thrombocytopenia
- Idiopathic neutropenia

Joints (*see* Differential Diagnosis for Immune-Mediated Arthritis)

Skin (*see* Autoimmune Skin Diseases)

Eye
- Uveitis
- Retinitis

Kidney
- Glomerulonephritis

Respiratory Tract
- Allergic rhinitis
- Allergic bronchitis (asthma)
- Pulmonary infiltrates with eosinophils

Gastrointestinal Tract
- Feline stomatitis, gingivitis
- Lymphocytic, plasmacytic enteritis
- Anal furunculosis (perianal fistula)

Neurologic System
- Myasthenia gravis
- Myositis
- Polyradiculoneuritis
- Granulomatous meningoencephalitis
- Polyarteritis

Endocrine Glands
- Thyroiditis (hypothyroidism)
- Adrenalitis (hypoadrenocorticism)
- Insulitis (diabetes mellitus)

Multisystemic Immune Disease
- Systemic lupus erythematosus

Systemic Lupus Erythematosus (SLE)

Organs and Tissues Affected

Red blood cells
- Immune-mediated hemolytic anemia
- Pure red cell aplasia

Platelets
- Immune-mediated thrombocytopenia

Glomeruli
- Glomerulonephritis

Synovium
- Nonerosive polyarthritis

Blood vessels
- Vasculitis

Epidermis
- Dermatitis

Neutrophils
- Immune-mediated neutrophilia

Clotting factors
- Coagulopathy

Central nervous system
- Seizures, focal signs

Skeletal muscle/nerve end plate
- Polymyositis
- Polyneuritis
- Myasthenia gravis

Criteria for Diagnosis in Dogs and Cats

SLE is diagnosed when three or more of the following criteria are manifested simultaneously or at any time:

Antinuclear antibodies (ANAs)
- Abnormal ANA titer in the absence of drugs or infectious or neoplastic conditions known to be associated with abnormal titers

Cutaneous lesions
- Depigmentation, erythema, erosions, ulcerations, crusts, scaling, with biopsy findings consistent with SLE

Oral ulcers
- Oral or nasopharyngeal ulceration, usually painless

Arthritis
- Nonerosive, nonseptic arthritis involving two or more peripheral joints

Renal disorders
- Glomerulonephritis or persistent proteinuria in the absence of urinary tract infection

Anemia/thrombocytopenia
- Hemolytic anemia/thrombocytopenia in the absence of offending drugs

Leukopenia
- Low total white cell count

Polymyositis or myocarditis
- Inflammatory disease of skeletal or cardiac muscles

Serositis
- Presence of a nonseptic inflammatory cavity effusion (abdominal, pleural, or pericardial)

Neurologic disorders
- Seizures or psychosis in the absence of known disorders

Antiphospholipids
- Prolongation of activated partial thromboplastin time (APTT) that fails to correct with a 1:1 mixture of patient's and normal plasma, in the absence of heparin or fibrin degradation products (FDPs)

Infectious Disease

Anaplasmosis, Canine

Clinical Signs

Infection may be subclinical
Fever
Depression
Inappetence
Scleral injection
Lameness, stiffness, reluctance to move
Coughing (soft and nonproductive)
Lymphadenopathy
Splenomegaly
Neutrophilic polyarthritis (rare)
CNS signs?
Vomiting/diarrhea
May be more susceptible to other infections

Laboratory Abnormalities

Thrombocytopenia
Lymphopenia
Eosinopenia
Mild regenerative anemia
Hypoalbuminemia
Mild to moderately elevated hepatic enzymes

Bacterial Infections, Systemic

Differential Diagnosis

Leptospirosis

Hepatic dysfunction, renal dysfunction, fever, anterior uveitis, icterus

Coagulation abnormalities, vomiting/diarrhea, icterus, polyuria/polydipsia, anorexia

Some cases may be subclinical

Borreliosis (Lyme Disease)

Fever, inappetence/lethargy, lymphadenopathy, polyarthritis

Glomerulonephritis/acute, progressive renal failure, mild dermatologic lesions

Meningitis/encephalitis (rare), myocarditis

Mycobacteriosis

Often asymptomatic, skin lesions, dermal nodules, draining tracts, lymphadenopathy, bronchopneumonia, pulmonary nodules, hilar lymphadenopathy, vomiting, diarrhea secondary to intestinal malabsorption, feline leprosy

Brucellosis (Dogs)

Clinical signs may be mild to absent

Fever, lymphadenopathy

Epididymitis, scrotal enlargement, scrotal dermatitis, infertility in males

Abortion, early embryonic death, fetal resorption, in pregnant bitches

Discospondylitis

Rarely uveitis, glomerulonephritis, meningoencephalitis

Tetanus

Localized tetanus, especially cats; stiffness in a muscle of limb

Generalized tetanus stiff gait, outstretched or dorsally curved tails, extreme muscle rigidity, hypersensitivity to touch, light, and sounds

Ears erect, lips drawn back (sardonic grin), protrusion of globe, enophthalmos

Trismus (lockjaw), laryngeal spasm, regurgitation, megaesophagus leading to aspiration pneumonia, seizures

Botulism
Generalized lower motor neuron and parasympathetic dysfunction, cranial nerve signs, mentation is normal
Quadriplegia, megaesophagus, respiratory paralysis; may lead to death

Feline Plague *(Yersinia pestis)*
Spread by fleas
May show signs of bubonic, septicemic, and pneumonic plague
Depression
Cervical swellings, draining tracts
Dyspnea or cough

Mycoplasmosis/Ureaplasmosis (Cats)
Conjunctivitis, sneezing, mucopurulent nasal discharge, coughing, dyspnea, fever, lameness, swollen joints, subcutaneous abscessation

Members of the Order Rickettsiales of Clinical Importance in Dogs and Cats

Rickettsioses (Spotted Fever Group Rickettsiae)
Rickettsia rickettsii
Species of the following tick genera transmit spotted-fever group agents: *Dermacentor, Rhipicephalus, Haemaphysalis,* and *Amblyomma*

Ehrlichiosis (Canine)
Ehrlichia canis, E. chaffeensis, E. ewingii, E. muris, and *E. ruminantium*

Anaplasmosis (Canine and Feline)
Anaplasma phagocytophilium
Anaplasma platys (canine cyclic thrombocytopenia: mildly pathogenic)

Neorickettsiosis
Neorickettsia helminthoeca, N. risticii

Bartonellosis, Canine

Clinical Findings

- Many species of *Bartonella* are suspected to cause disease in dogs (e.g., *B. vinsonii, B. henselae, B. clarridgeae, B. elizabethae*)
- Fever
- Endocarditis, myocarditis, arrhythmias

- Epistaxis
- Intermittent lameness
- Bone pain
- Granulomatous lymphadenitis
- Dermatologic lesions/cutaneous vasculitis
- Anterior uveitis
- Polyarthritis
- Meningoencephalitis
- Immune-mediated hemolytic anemia
- Thrombocytopenia
- Eosinophilia
- Peliosis hepatitis
- Granulomatous hepatitis
- Chronic weight loss

Bartonellosis, Feline

Subclinical Disease in Most Cats

Uveitis?
Endocarditis?

Anaplasmosis

Anaplasma phagocytophilum, formally known as *Ehrlichia equi, E. phagocytophila*

Cause of Canine Granulocytic Ehrlichiosis

Clinical Signs

Fever
Depression
Inappetence
Scleral injection
Lameness/polyarthritis
Coughing
Lymphadenopathy
Splenomegaly
Vomiting/diarrhea
Lymphopenia, eosinopenia, mild nonregenerative anemia
Hypoalbuminemia, elevated hepatic enzymes

Anaplasma Platys

Cause of Canine Thrombocytic Anaplasmosis

Forms morula that can be visualized in platelets

Clinical Signs

Majority of cases in United States have been mild or subclinical

More severe signs in European or South American cases include:

- Fever
- Splenomegaly
- Hemorrhage

Ehrlichiosis, Canine

Clinical Findings

Acute

Fever
Anorexia/weight loss
Depression
Serous or purulent oculonasal discharge
Lymphadenopathy/splenomegaly
Peripheral edema
Petechial and ecchymotic hemorrhages
Neurologic signs (ataxia, seizures, vestibular signs, hyperesthesia, cranial nerve defects)
Dyspnea
History of recent or present tick bite
Thrombocytopenia
Leukopenia followed by leukocytosis and monocytosis
Low-grade nonregenerative anemia, unless hemorrhage
Variable *Ehrlichia* titer, polymerase chain reaction (PCR) positive

Subclinical

No clinical abnormalities apparent
Hyperglobulinemia, thrombocytopenia, neutropenia, lymphocytosis, monocytosis
Positive *Ehrlichia* titer, PCR positive

Chronic

Depression
Pale mucous membranes
Weight loss
Abdominal pain
Splenomegaly
Epistaxis, retinal hemorrhage, petechia and ecchymoses, melena, hematochezia, hematuria, and other examples of hemorrhage
Lymphadenopathy
Stiffness, swollen/painful joints, polymyositis
Hepatomegaly
Dyspnea, interstitial or alveolar lung infiltrates

Perivascular retinitis, hyphema, retinal detachment, anterior uveitis, corneal edema
Seizures, paresis, meningeal pain, cranial nerve deficits
Arrhythmias
Polyuria/polydipsia
Secondary opportunistic infection (viral papillomatosis, protozoal infections, bacteriuria)
Monocytosis, lymphocytosis, thrombocytopenia, nonregenerative anemia, hyperglobulinemia, hypoalbuminemia, hypocellular bone marrow, proteinuria, polyclonal or monoclonal gammopathy, nonseptic suppurative polyarthritis, cerebrospinal fluid (CSF) mononuclear pleocytosis
Increased alanine aminotransferase (ALT) and alkaline phosphatase (ALP)
Positive *Ehrlichia* titer, PCR positive

Influenza, Canine

Clinical Features

- Most outbreaks in group housed dogs (race tracks, animal shelters)
- Individual pets often had a recent history of exposure to other dogs
- Mild form may cause a harsh cough similar to cough heard with infectious tracheobronchitis
- More commonly cough is soft and moist, cough may persist for as long as a month
- Fever
- Mucopurulent nasal discharge
- Increased respiratory rate progressing to respiratory distress
- May progress to overt pneumonia
- Mortality rate less than 5%. Very young and very old are most at risk

Neorickettsiosis Canine

Neorickettsia helminthoeca (salmon poisoning disease)
Restricted to western slopes of Cascade Mountains from northern California to southern Vancouver Island
Vector is a fluke *Nanophyetus salmincola*. Dogs become infected from ingesting parasitized fish.

Clinical Signs

Fever
Anorexia/weight loss
Depression
Lymphadenopathy

Vomiting
Diarrhea
Hematochezia
Neutrophilia with left shift, lymphopenia, monocytosis, thrombocytopenia
Electrolyte derangements, elevated hepatic enzymes, hypoalbuminemia
Neorickettsia risticii
Cause of equine Potomac horse fever
Vector is suspected to be a fluke *Acanthatrium oregonense*
Has been identified by culture and PCR in dogs with the following signs:
Lethargy
Intermittent vomiting
Bleeding tendencies
Polyarthritis
Neurologic signs
Dependent edema
Anemia
Thrombocytopenia

Mycoses, Systemic

Clinical Findings

Blastomycosis

Restricted primarily to Mississippi, Ohio, Missouri, Tennessee, and St. Lawrence River valleys plus the southern Great Lakes and the southern Mid-Atlantic states
Sporting breeds predisposed because of greater exposure, males more than females
Anorexia, depression, weight loss, cachexia, fever, mild to severe dyspnea, cyanosis, cough, chylothorax, diffuse lymphadenopathy, papules, plaques and ulcerative nodules, paronychia, chorioretinitis, conjunctivitis, keratitis, iridocyclitis, anterior uveitis, subretinal granulomas, retinal detachment, secondary glaucoma, lameness from osteomyelitis, splenomegaly
Radiographically, infiltrative bronchointerstitial and alveolar disease, hilar lymphadenopathy

Histoplasmosis

Restricted primarily to Mississippi, Missouri, and Ohio River valleys and Mid-Atlantic states
Sporting breeds predisposed because of greater exposure
Common clinical signs include anorexia, fever, depression, weight loss, cough, dyspnea, diarrhea (large bowel diarrhea most often, may see protein-losing

enteropathy), hepatosplenomegaly, icterus, ascites, and lymphadenopathy.

Less common signs include lameness secondary to osteomyelitis or polyarthritis, chorioretinitis, central nervous system (CNS) disease, and cutaneous lesions.

Differential Diagnosis for Gastrointestinal Signs Seen in Dogs and Cats with Histoplasmosis

Large Intestinal Disease

Diet-Associated Colitis
- Dietary hypersensitivity
- Foreign material–induced colitis

Idiopathic Colitis
- Lymphocytic-plasmacytic colitis
- Eosinophilic colitis
- Granulomatous colitis
- Histiocytic ulcerative colitis of Boxer dogs
- Suppurative colitis

Parasitic and Protozoal Colitis
- Trichuriasis (whipworm)
- Ancylostomiasis (hookworm)
- Entamebiasis
- Balantidiasis
- Giardiasis

Bacterial colitis
- Salmonellosis
- Campylobacter jejuni
- Yersinia enterocolitica, Y. pseudotuberculosis
- Mycobacteria
- Clos*tridium perfringens, C. difficile*

Fungal colitis
- Candidiasis
- GI pythiosis
- Prototheco sis

Cecocolic or ileocolic intussusception

Pancreatitis-associated colitis

Small Intestinal Disease

Idiopathic inflammatory bowel disease
- Lymphocytic-plasmacytic enteritis
- Eosinophilic enteritis
- Granulomatous enteritis

Intestinal lymphosarcoma

Parasitic enteritis
- Ancylostomiasis
- Toxocariasis
- Chronic giardiasis

Infectious enteritis
- Small intestinal bacterial overgrowth
- GI pythiosis

Lymphangiectasia
Exocrine pancreatic insufficiency
Partial intestinal obstruction
Chronic enteropathy of Shar-Peis
Immunoproliferative enteritis of Basenjis

Coccidioidomycosis

Primarily southwestern United States, California, Mexico, Central and South America

Common clinical signs include lameness with swollen and painful joints and bones, cough, dyspnea, anorexia, weakness, pleural effusion, and cutaneous lesions over infected bones.

Less common signs include myocarditis, icterus, renomegaly, splenomegaly, hepatomegaly, orchitis, epididymitis, keratitis, iritis, granulomatous uveitis, glaucoma, seizures, ataxia, and central vestibular disease.

Cryptococcosis

Found worldwide, more common in southern United States, most common in cats

Common clinical signs include upper respiratory signs, unilateral to bilateral nasal discharge, soft masses in nasal cavity or over bridge of nose, ulcerative skin lesions, lymphadenopathy, granulomatous chorioretinitis, and retinal detachment.

Less common signs include fever, lung involvement, CNS involvement caused by invasion through cribriform plate, depression, seizures, circling, ataxia, blindness, head pressing, and paresis.

Aspergillosis

Dogs affected more often than cats

Nasal turbinate destruction, frontal sinus osteomyelitis, mucoid to hemorrhagic nasal discharge, epistaxis

May lead to masticatory muscle atrophy and CNS disease by erosion through cribriform plate

In rare cases, disseminates and causes multiple-organ disease

Pythiosis, Lagenidiosis (*Pythium insidiosum*, *Lagenidium giganteum*)

Severe, often fatal, chronic gastrointestinal and cutaneous diseases

Zygomycosis (Multiple Fungi in Class Zygomycetes)

Nasopharyngeal involvement, poorly responsive to therapy

Differential Diagnosis for Systemic Manifestations

Multisystemic granulomatous, neoplastic, and immune-mediated diseases must be differentiated from disseminated systemic mycoses.

Differential Diagnosis for Nodular Skin Disease

Bacteria Skin Disease

- Actinomycosis
- Mycobacteriosis
- Botryomycosis
- Brucellosis
- *Rhodococcus equi* infection
- *Bartonella vinsonii* subsp. *Berkhoffi* infection

Mycotic and Miscellaneous Infectious Skin Disease

- Cryptococcosis
- Blastomycosis
- Coccidioidomycosis
- Sporotrichosis
- Basidiobolomycosis
- Conidiobolomycosis
- Phaeohyphomycosis
- Hyalohyphomycosis
- Eumycotic mycetoma
- Dermatophytic mycetoma
- Protothecosis
- Pythiosis
- Lagenidiosis
- Nodular leishmaniasis

Noninfectious Pyogranulomatous Skin Disease

- Foreign body reaction
- Idiopathic nodular panniculitis
- Sebaceous adenitis (nodular form)
- Canine cutaneous sterile pyogranulomatous/granuloma syndrome

Neoplasia

- Squamous cell carcinoma
- Cutaneous lymphoma
- Mycosis fungoides (cutaneous T-cell lymphoma)
- Cutaneous histiocytosis

Miscellaneous Diseases

- Systemic lupus erythematosus
- Systemic vasculitis
- Cutaneous embolic disease

Differential Diagnosis for Chorioretinitis, Exudative Retinal Detachment, and Panophthalmitis

Fungal

- Blastomycosis
- Cryptococcosis
- Coccidioidomycosis
- Geotrichosis
- Histoplasmosis
- Aspergillosis

Neoplasia

- Lymphosarcoma
- Metastatic neoplasia

Miscellaneous Infectious Causes

- Protothecosis
- Brucellosis
- Toxoplasmosis
- *Neosporum caninum* infection
- Leishmaniasis

Lymphadenopathy must be differentiated from numerous causes including lymphosarcoma, other fungal infections, rickettsial diseases, brucellosis, mycobacteriosis, protothecosis, and leishmaniasis.

Solitary bone lesions must be differentiated from primary or metastatic neoplasia and other fungal or bacterial osteomyelitis.

Polysystemic Protozoal Diseases

Clinical Findings

Feline Toxoplasmosis

Acute toxoplasmosis: may induce a self-limiting, small bowel diarrhea

Disseminated toxoplasmosis: overwhelming intracellular replication of tachyzoites after primary infection—depression, anorexia, fever, hypothermia, peritoneal effusion, icterus, dyspnea, death—coinfection with feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis (FIP), and others may predispose to disseminated toxoplasmosis

Chronic toxoplasmosis: anterior or posterior uveitis, fever, muscle hyperesthesia, weight loss, anorexia, seizures, ataxia, icterus, diarrhea, pancreatitis

Canine Toxoplasmosis

Respiratory, gastrointestinal, neuromuscular signs: fever, vomiting, diarrhea, dyspnea, icterus, ataxia, seizures, tremors, cranial nerve deficits, paresis, paralysis, myositis, lower motor neuron disease, myocardial disease, chorioretinitis, anterior uveitis, iridocyclitis, optic neuritis (ocular lesions less common in dogs than cats)

Neosporosis

Most common in neonates but can be seen at any age

Ascending paralysis, hyperextension of hind limbs, muscle atrophy, polymyositis, multifocal CNS disease, myocarditis, dysphagia, ulcerative dermatitis, pneumonia, hepatitis

Babesiosis

Anemia, fever, pale mucous membranes, tachycardia, tachypnea, depression, anorexia, weakness, icterus, petechiae, hepatosplenomegaly, disseminated intravascular coagulation (DIC), metabolic acidosis, renal disease

Cytauxzoonosis

Fever, anorexia, dyspnea (pneumonitis), depression, icterus, pale mucous membranes, death

Hepatozoonosis (*Hepatozoon canis* and *H. americanum*)

Most common in puppies and immunosuppressed dogs, but *H. americanum* can be primary

Fever, weight loss, severe hyperesthesia, anorexia, anemia, depression, oculonasal discharge, bloody diarrhea

Leishmaniasis

Weight loss, normal to increased appetite, polyuria/polydipsia, muscle wasting, depression, vomiting, diarrhea, cough, epistaxis, sneezing, melena, splenomegaly, facial alopecia, rhinitis, dermatitis, icterus, swollen and painful joints, uveitis, conjunctivitis

Dermatologic lesions include hyperkeratosis, scaling, mucocutaneous ulcers, and intradermal nodules on muzzle, ears, and footpads.

American Trypanosomiasis *(Trypanosoma cruzi)*

Acute infection: myocarditis, heart failure—lymphadenopathy, pale mucous membranes, tachycardia, pulse deficits, hepatomegaly, abdominal distension, anorexia, diarrhea, neurologic signs

Chronic infection: Those that survive acute infection may present with chronic dilative cardiomyopathy—right-sided heart failure, conductive disturbances, supraventricular arrhythmias.

Rocky Mountain Spotted Fever

Clinical Findings

Depression/lethargy
Fever
Anorexia
Myalgia/arthralgia
Lymphadenopathy
Vestibular deficits
Conjunctivitis/scleral congestion/hyphema/iridal and retinal hemorrhage
Pneumonitis/dyspnea/cough
Abdominal pain
Edema of face and extremities
Epistaxis
Melena
Hematuria
Anterior uveitis
Rash/petechiae
Nausea/vomiting
Diarrhea
Vasculitis/thrombocytopenia/disseminated intravascular coagulation (DIC)
Hyperesthesia/spinal cord signs
Seizures
Cardiac arrhythmias
Icterus
Acute renal failure
Coma/stupor
Polyuria/polydipsia

Sepsis and Systemic Inflammatory Response Syndrome (SIRS)

Definitions

Bacteremia: the presence of viable bacteria in the bloodstream
Sepsis: infection-induced systemic inflammation
Severe sepsis: organ dysfunction and manifestations of hypoperfusion or hypotension secondary to sepsis
Septic shock: hypotension secondary to sepsis, not responsive to intravenous (IV) fluid therapy
SIRS: systemic inflammation caused by either infectious or noninfectious processes. Diagnosis of SIRS is based on fulfillment of at least two of four criteria (tachycardia,

tachypnea, hypothermia, or hyperthermia and either leucocytosis, leucopenia, or bands)

Multiple organ dysfunction syndrome (MODS): altered function of two or more organs secondary to SIRS such that homeostasis cannot be maintained without intervention

Acute respiratory distress syndrome (ARDS): a pulmonary inflammatory disorder characterized by noncardiogenic pulmonary edema, neutrophilic inflammation, and hypoxemia

Noninfectious Causes of SIRS

Pancreatitis
Tissue trauma
Heat stroke
Ischemia
Burns
Pansystemic neoplasia

Infectious Causes of SIRS (Sepsis)

Peritonitis
Pyometra
Prostatitis
Prostatic abscess
Pyelonephritis
Pneumonia
Pyothorax
Gastroenteritis
Endocarditis
Nosocomial infections (IV catheters, urinary catheters, etc.)

Clinical Findings of Sepsis and SIRS

Fever or hypothermia
Tachycardia, tachypnea
Neutrophilia with left shift or leukopenia
Anemia
Depression
Bounding or diminished pulses
Brick-red mucus membranes or pallor
Hypothermia
Thrombocytopenia
Hypoalbuminemia, hypoglycemia
Disseminated intravascular coagulation (DIC)
Bilirubinemia
Elevated hepatic enzymes
Azotemia
Oliguria

Lactic acidosis
Hypoxemia
Signs related to underlying condition

Vaccines, Recommended Core vs. Noncore

Core Vaccines for Dogs

- Distemper
- Parvovirus
- Adenovirus-2
- Rabies

Core Vaccines for Cats

- Parvovirus (panleukopenia)
- Herpesvirus-1
- Calicivirus
- Rabies

Noncore Vaccines for Dogs

Need determined by individual clinician after assessment of patient risk

- Bordetellosis
- Parainfluenza
- Canine influenza
- Leptospirosis
- Lyme borreliosis
- *Crotalus atrax*
- *Porphyromonas* spp.

Noncore Vaccines for Cats

Need determined by individual clinician after assessment of patient risk

- Feline leukemia virus (FeLV)
- Feline immunodeficiency virus (FIV)
- *Chlamydophila felis* (formally, *Chlamydia psittaci*)
- Bordetellosis

Viruses, Canine

Common Viral Agents of Diseases of Dogs

Parvovirus

May be asymptomatic or fulminant disease
Anorexia, lethargy, fever, vomiting, hemorrhagic diarrhea, myocarditis (rare)
Worse in very young and parasitized puppies
Neutropenia, hypoalbuminemia, severe dehydration, secondary septicemia

Coronavirus
- Diarrhea (infrequently blood in feces), vomiting, anorexia, lethargy, often self-limiting
- Canine respiratory coronavirus, part of "kennel cough" complex
- Coughing, sneezing, nasal discharge
- Canine pancytotropic coronavirus
- Severe clinical disease in puppies and juvenile dogs
- Fever, lethargy, anorexia, vomiting, hemorrhagic diarrhea, ataxia, seizures

Rotavirus
- Vomiting, diarrhea (rarely bloody), anorexia, typically recover after 5-7 days

Adenovirus Type 1 (Infectious Canine Hepatitis)
- Fever, anorexia, lethargy, depression, abdominal pain, pale mucous membranes, tonsillitis, pharyngitis, coughing, hepatomegaly
- Severe cases: coagulation abnormalities, petechiae, ecchymosis, DIC, rarely icterus, hepatic encephalopathy
- Anterior uveitis and glomerulonephritis secondary to immune complex deposition

Canine Distemper Virus (*See* the next section)

Canine Influenza A Subtype H3N8 Virus
- Acute onset of coughing, sneezing, nasal discharge, ocular discharge
- Lowgrade fever
- Secondary commensal bacterial infections leading to mucopurulent discharge and productive cough
- May lead to pneumonia with high fever, inappetence, productive cough, and increased respiratory effort

Rabies Virus
- Variable incubation period, prodromal phase: nervousness, anxiety, paresthesia
- Progress to forebrain signs ("furious" form of rabies): irritability, restlessness, pica, photophobia, increased saliva production with decreasing ability to swallow, hyperesthesia progressing to incoordination, seizures, and death
- May also progress to "dumb" form: paralysis, lower motor disease, leading to coma, respiratory paralysis, and death

Pseudorabies
- Suspected to be result from ingestion of infected raw pork

Neurologic dysfunction: ataxia, abnormal papillary light response, restlessness, trismus, cervical rigidity, ptyalism, tachypnea, excoriation from pruritus of head and neck; vomiting, diarrhea; most dogs die within 48 hours

Parainfluenza and Adenovirus Type 2

Hacking cough with gagging, easily elicited with tracheal palpation; cough may be paroxysmal, usually subsides within 7-10 days, and may lead to secondary bacterial or mycoplasmal infection

Canine Herpesvirus

Abortion, stillbirths; puppies born live progress to crying, hypothermia, soft stools, petechiae, cessation of nursing, and death

Older puppies develop mild respiratory signs that may emerge later as neurologic disease (ataxia, blindness, central vestibular disease).

Adult dogs: usually asymptomatic, rhinitis, pharyngitis, vaginal or preputial hyperemia, hyperplasia of vaginal mucosal lymphoid follicles, submucosal hemorrhage

Canine Oral Papillomavirus

Oral papilloma (warts), may be quite extensive, spontaneously regress

West Nile Virus

Clinical disease is uncommon.

Bornavirus

Seropositivity in the absence of clinical signs appears possible.

Tremors, salivation, mydriasis, circling

Canine Distemper Virus Infection, Clinical Findings

General Signs

Fever
Lethargy
Depression
Anorexia
Dehydration

Respiratory Tract

Mucoid to mucopurulent discharge
Bronchopneumonia

- Coughing
- Crackles on auscultation
- Increased bronchovesicular sounds
- Dyspnea

Sneezing

Gastrointestinal Tract
Vomiting
Small bowel diarrhea

Ocular Disease
Mucopurulent ocular discharge
Chorioretinitis, medallion lesions, optic neuritis, retinal detachment
Keratoconjunctivitis sicca
Anterior uveitis

Neurologic Disease
Spinal cord lesion: paresis and ataxia
Central vestibular disease: head tilt, nystagmus, other cranial nerve and conscious proprioception deficits
Cerebellar disease: ataxia, head bobbing, hypermetria
Cerebral disease: seizures, blindness
Chorea myoclonus: rhythmic jerking of single muscles or muscle groups

Miscellaneous
Tonsillar enlargement
Pustular dermatosis
Hyperkeratosis of nose and footpads
Enamel hypoplasia

In Utero Infection
Stillbirth
Abortion
"Fading puppy" syndrome in neonatal period
Central nervous system signs at birth

Viruses, Feline

American Association of Feline Practitioners Guidelines for Retroviral Testing in Cats

- Sick cats should be tested even if they have tested negative before.
- Cats and kittens should be tested when they are first acquired.
- Even cats not expected to live with other cats should be tested. This provides a health assessment of the individual, other cats may join the household, indoor cats may escape and expose other cats.
- Tests should be performed at adoption and negative cats should be retested a minimum of 60 days later.

- Cats with known recent exposure to a retrovirus-infected cat or a cat with unknown status, particularly via a bite wound, should be tested regardless of previous test results. Testing should be done immediately and, if negative, should be repeated after a minimum of 30 days for FeLV and after a minimum of 60 days for FIV (when the type of potential viral exposure is unknown, retesting for both viruses after 60 days is most practical).
- Cats living in households with other cats infected with FIV or FeLV should be tested annually.
- High-risk cats (cats in cat-dense neighborhoods or cats that fight and get cat-bite wounds and abscesses) should be tested regularly.
- Cats should be tested before initial vaccination against FeLV or FIV.
- Cats used for blood or tissue donation should have negative screening tests for FeLV and FIV and should be negative for real-time PCR tests.
- Intermittent retesting is not necessary for cats with confirmed negative infection status unless there is opportunity for exposure to infected cats or if they become ill.
- Each cat should be individually tested. Testing of one cat as a proxy for another or pooling samples from multiple cats for testing is inappropriate.

Clinical Signs of Rabies Virus Infection in Cats

- Initially signs are nonspecific: lethargy, inappetence, vomiting, diarrhea
- Rapid and continual deterioration of clinical conditions, no waxing and waning
- Behavioral changes: more reclusive or attention-seeking, may unpredictably attack animate, inanimate, or unseen objects
- Irrevocable progression to classic signs, ptyalism with decreased ability to swallow leads to contamination of oral cavity, chin, and forelegs with potentially infectious saliva. Cranial nerve signs such as anisocoria, pupil dysfunction, facial or tongue paresis, and changes in phonation may occur.
- Auditory, visual, or tactile stimulation may elicit profound aggression to self-mutilation.
- Become profoundly moribund to comatose to death. 100% fatal

Feline Infectious Peritonitis (FIP, Feline Coronavirus Infection), Clinical Findings

Signalment and History

- Purebred cats from cattery
- Multicat households
- Younger than 5 years or older than 10 years of age
- Previous history of mild, self-limiting gastrointestinal or respiratory disease
- Anorexia, weight loss, depression
- Seizures, nystagmus, ataxia
- Acute, fulminant course in cats with effusive FIP
- Chronic, intermittent course in cats with noneffusive FIP

Physical Examination Findings

- Fever
- Weight loss
- Abdominal distension/fluid wave
- Abdominal mass (focal intestinal granuloma, lymphadenopathy)
- Icterus
- Muffled heart or lung sounds
- Dyspnea secondary to pleural effusion
- Hepatomegaly
- Chorioretinitis, iridocyclitis
- Splenomegaly
- Pale mucous membranes with or without petechiae
- Multifocal neurologic abnormalities
- Irregularly marginated kidneys
- Renomegaly

Clinicopathologic Abnormalities

- Complete blood count (CBC): nonregenerative anemia, neutrophilia with or without left shift, lymphopenia
- Serum chemistry: elevated alkaline phosphatase (ALP) and alanine aminotransferase (ALT), hyperbilirubinemia, hyperglobulinemia (polyclonal, rarely monoclonal gammopathy), azotemia (prerenal or renal)
- Urinalysis: proteinuria
- Nonseptic, pyogranulomatous exudate in peritoneal cavity, pleural space, and pericardium
- Positive coronavirus antibody titer (especially in noneffusive cases)
- Cerebrospinal fluid (CSF) tap: increased protein concentration, neutrophilic pleocytosis, coronavirus antibodies
- Histopathology: pyogranulomatous inflammation in perivascular locations of tissues

Positive for coronavirus on immunofluorescence or reverse-transcriptase polymerase chain reaction (RT-PCR) testing of abdominal or pleural effusions (although these tests do not differentiate between FIP-causing viruses and "harmless" feline enteric coronavirus)

Feline Immunodeficiency Virus (FIV) Infection, Clinical Findings

Primary Phase of Infection

Low-grade fever
Lymphadenopathy
Neutropenia

Latent Phase

No clinical signs for months to years

Immunodeficiency Phase

Primary Viral Effects

Weight loss
Nonregenerative anemia, neutropenia, thrombocytopenia
Small bowel diarrhea
Glomerulonephritis
Myeloproliferative disorders
Lymphoma
Renal failure
Anterior uveitis, pars planitis
Behavioral abnormalities

Opportunistic Infectious Agents

Cutaneous: atypical mycobacteriosis, demodicosis, *Notoedres* and *Otodectes* infestation, dermatophytosis, cryptococcosis, cowpox
Gastrointestinal: cryptosporidiosis, coccidiosis, giardiasis, salmonellosis, campylobacteriosis, others
Renal: bacterial infections, FIP, feline leukemia virus (FeLV)
Urinary tract: bacterial infections
Neoplasia: FeLV
Hematologic: *Mycoplasma haemofelis,* FeLV, bartonellosis
Neurologic: toxoplasmosis, cryptococcosis, FIP, FeLV
Ophthalmologic: toxoplasmosis, FIP, cryptococcosis, herpesvirus, bartonellosis
Pneumonia/pneumonitis: bacterial, toxoplasmosis, cryptococcosis

Pyothorax: bacterial
Stomatitis: calicivirus, bacterial, candidiasis, bartonellosis
Upper respiratory: herpesvirus, calicivirus, bacterial, cryptococcosis

Feline Leukemia Virus (FeLV), Clinical Findings

Acute Phase
- Fever
- Malaise
- Diarrhea
- Leukopenia

General Signs
- Anorexia
- Weight loss
- Depression
- Many FeLV positive cats are asymptomatic at diagnosis

Neoplastic
- Lymphoma: mediastinal, multicentric, alimentary, renal
- Leukemia: lymphocytic, myelogenous, erythroid, megakaryocytic
- Myeloproliferative disorders
- Fibrosarcoma

Icterus
- Prehepatic: immune-mediated red blood cell (RBC) destruction induced by FeLV or secondary infection with *Mycoplasma haemofelis*
- Hepatic: hepatic lymphoma, focal liver necrosis, hepatic lipidosis
- Posthepatic: alimentary lymphoma

Bone marrow
- Pure red cell aplasia
- Regenerative anemia (less common and often associated with coinfection with *Mycoplasma haemofelis*)
- Myeloproliferative disease (anemia, leukopenia, thrombocytopenia)

Stomatitis
- Bacterial infection
- Calicivirus infection

Rhinitis/Pneumonia
- Bacteria
- Herpesvirus and calicivirus

Renal
Glomerulonephritis
Renal failure
Urinary incontinence: sphincter incompetence or detrusor hyperactivity

Ocular Lymphoma
Aqueous flare, mass lesions, keratitic precipitates, lens luxations, glaucoma, anterior uveitis

Neurologic Polyneuropathy or lymphoma
Anisocoria, ataxia, weakness, tetraparesis, paraparesis, behavioral changes, urinary incontinence
Secondary infection with FIP, *Toxoplasma gondii, Cryptococcus neoformans*

In Utero Infection
Abortion, stillbirth, infertility, kitten mortality complex ("fading kitten" syndrome)

Lameness
Neutrophilic polyarthritis secondary to immune complex deposition
Multiple cartilaginous exostoses

Feline Leukemia Virus, Possible Outcomes Following Exposure

Progressive Infection
Viral replication in lymphoid tissue and bone marrow, spread to mucosal and glandular tissues, leading to shedding of virus. Most cats become persistently infected and frequently die of an FeLV-associated disease within a few years.

Regressive Infection
Effective immune response limits viral replication. FeLV antigen detectable in peripheral blood within 2-3 weeks after exposure but disappears 2-8 weeks later. May not ever develop antigenemia. Clinical relevance of regressive infection is not clear. May have persistent integration of FeLV DNA in their genome but are unlikely to develop FeLV-associated diseases. Do not shed virus.

Abortive Exposure
Seen infrequently following experimental FeLV inoculation characterized by negative results for culturable virus, antigen, viral RNA, and proviral DNA

Focal Infections
Rare events in which cats have FeLV infection restricted to certain tissues such as spleen, lymph nodes, small intestine, or mammary glands.

Other Feline Viral Diseases

Upper Respiratory Tract Viruses

- Herpesvirus type 1: ocular and nasal disease
- Calicivirus: ocular, nasal, and oral disease; rarely joint disease
- Reovirus: Conjunctivitis, respiratory lesions, diarrhea experimentally, no evidence of importance in the field

Enteric Viruses

- Feline parvovirus (panleukopenia virus): enteritis, panleukopenia, cerebellar hypoplasia, fetal death
- Feline coronavirus: mild enteritis, FIP
- Rotavirus: rare cause of mild diarrhea
- Astrovirus: uncommon cause of persistent watery diarrhea
- Torovirus: may be associated with protruding nictitating membrane and diarrhea syndrome

Miscellaneous

- Cowpox virus: mainly see skin lesions; sporadic disease in cats Hantavirus: zoonotic disease of wild rodents; clinical significance in cats not known
- Rabies virus
- Pseudorabies virus: cats are a rare host, severe behavioral changes, pruritus, paralysis, coma, death
- Feline herpesvirus type 2: possible association with feline idiopathic lower urinary tract disease

Joint and Bone Disorders

Arthritis

Differential Diagnosis: Infectious Arthritis

Septic Arthritis

Bacterial Suppurative Arthritis

Penetrating wounds
- Animal bites

Iatrogenic
- Infection during surgery, arthrocentesis

Trauma (e.g., hit by car)

Hematogenous
- Endocarditis
- Omphalophlebitis
- Pyoderma
- Other foci of infection

Lyme Arthritis

Borrelia burgdorferi
Transmitted by *Ixodes* ticks

Bacterial L-Form Arthritis

Cell wall–deficient bacteria
Causes suppurative arthritis and subcutaneous abscesses in cats

***Mycoplasma* Arthritis**

Debilitated and immunosuppressed animals
M. gatae, M. felis in cats

Fungal Arthritis (Rare)

Coccidioides immitis
Blastomyces dermatitidis
Cryptococcusneoformans
Sporothrix schenckii
Aspergillus terreus

Rickettsial Arthritis
- Rocky Mountain spotted fever *(Rickettsia rickettsii)*
- *Ehrlichia canis*
- *Anaplasma phagocytophilium*

Protozoal Arthritis
- Leishmaniasis (*Leishmania* spp.)
- Toxoplasmosis (rare)
- Neosporosis *(Neospora caninum):* polyarthritis, polymyositis, neurologic disease
- Hepatozoonosis: polyarthritis and polymyositis in dog and cat
- Babesiosis (rare, more often causes severe anemia)

Viral Arthritis
- Calicivirus infection in cats

Differential Diagnosis of Noninfectious Arthritis

Nonerosive
- Immune-mediated polyarthritis
- Systemic lupus erythematosus
- Reactive polyarthritis (bacterial, fungal, parasitic, neoplastic, enterohepatic, drug reaction, vaccine induced)
- Breed-associated syndromes
  - Polyarthritis (Akita, Newfoundland, Weimaraner)
  - Polyarthritis/meningitis (Akita, Beagle, Bernese Mountain Dog, Boxer, German Shorthair Pointer)
  - Polyarthritis/polymyositis (spaniels)
  - Familial Shar-Pei fever
- Lymphoplasmacytic synovitis

Erosive
- Rheumatoid-like arthritis
- Erosive polyarthritis of Greyhounds
- Feline chronic progressive polyarthritis

Bone Disorders

Differential Diagnosis: Congenital, Developmental, Genetic

Congenital
- Hemimelia, phocomelia, amelia: absence of portions or entire limb (amelia)
- Syndactyly: fusion of two or more digits; rarely clinically significant

Polydactyly: extra digits
Ectrodactyly: third metacarpal and digit missing forming a cleft (split or "lobster" claw)
Segmented hemiatrophy: limb hypoplasia

Developmental and Genetic

Osteopetrosis: rare; diaphysis remains filled with bone, marrow does not form, fragile bones
Osteogenesis imperfecta: heritable diseases—fragile bones
Mucopolysaccharidosis: rare lysosomal storage disease—Siamese cats—causes dwarfism, facial dysmorphism
Dwarfism
- Osteochondrodysplasias
- Pituitary dwarfism
- Congenital hypothyroidism

Retained cartilage cores
Craniomandibular osteopathy (West Highland White Terrier, Scottish Terrier, Cairn Terrier, Boston Terrier, other terriers)
Multiple cartilaginous exostoses

Differential Diagnosis: Metabolic, Nutritional, Endocrine, Idiopathic

Metabolic

Nutritional secondary hyperparathyroidism
Lead poisoning

Nutritional

Rickets (hypovitaminosis D)
Renal osteodystrophy
Hypervitaminosis A: causes osteopathy
Hypovitaminosis A: deformed bones secondary to impedance of bone remodeling
Hypervitaminosis D: skeletal demineralization
Zinc-responsive chondrodysplasia
Copper deficiency
Overnutrition of growing dogs

Endocrine

Primary hyperparathyroidism
Humoral hypercalcemia of malignancy
Hyperadrenocorticism
Hypogonadism: delay in physis closure after early gonadectomy
Hepatic osteodystrophy
Anticonvulsant osteodystrophy

Idiopathic

- Enostosis (panosteitis)
- Metaphyseal osteopathy (hypertrophic osteodystrophy)
- Avascular necrosis of femoral head (Legg-Calvé-Perthes disease)
- Secondary hypertrophic osteopathy (usually in response to thoracic neoplasia)
- Medullary bone infarction
- Bone cyst
- Aneurysmal bone cyst
- Subchondral bone cyst
- Fibrous dysplasia
- Central giant cell granuloma

SECTION IX

Liver and Exocrine Pancreatic Disorders

Cholangitis and Cholangiohepatitis, Feline

Comparative Clinical Findings

Suppurative (Neutrophilic) Cholangitis and Cholangiohepatitis

- Middle-aged to older cats
- Often depressed and ill
- Anorexia (usually)
- Jaundice
- Neutrophilia
- Increased alanine aminotransferase (ALT)
- Increased alkaline phosphatase (ALP)
- Increased bilirubin (±)
- Increased serum and urine bile acids (±)
- Hyperechoic liver and bile stasis
- Primarily neutrophilic infiltrate
- Lesions surround bile ducts
- May be associated with pancreatitis and/or inflammatory bowel disease
- Respond to antibiotics and supportive nonspecific treatments

Lymphocytic Cholangitis

- Younger cats
- Persians
- Bright and alert
- Polyphagia (±)

Ascites (±)
Icterus (±)
Lymphadenopathy (±)
Hepatomegaly (±)
Neutrophilia (±)
Lymphopenia (±)
Bile acids (±)
Increased ALT
Increased ALP
Bilirubinemia/bilirubinuria (±)
Hyperglobulinemia
Hyperechoic liver (±)
Primarily lymphocytic infiltrate
Lesions found in portal areas
Variable fibrosis
Pancreatitis (may be present)
Positive response to immunosuppressive corticosteroids

Exocrine Pancreatic Disease

Differential Diagnosis

Pancreatitis
- Acute
- Chronic

Exocrine pancreatic insufficiency
Pancreatic pseudocyst
Pancreatic abscess
Exocrine pancreatic neoplasia
- Pancreatic adenoma
- Pancreatic adenocarcinoma
- Pancreatic sarcoma (spindle cell sarcoma, lymphosarcoma) rare

Nodular hyperplasia
Pancreatic parasites (cats)
- *Eurytrema procyonis* (pancreatic fluke)
- *Amphimerus pseudofelineus* (hepatic fluke)

Pancreatic bladder
- Abnormal extension of pancreatic duct (rare finding in cat)

Clinical Findings of Exocrine Pancreatic Insufficiency

Most often seen in young to middle-aged dogs; German Shepherds are predisposed
Chronic weight loss

Ravenous appetite
Coprophagia
Pica
Change in fecal character
- Voluminous
- Soft
- Watery
- May be normal

Poor haircoat quality
Borborygmus, flatulence
Coagulation disorder (caused by malabsorption of vitamin K, rare)

Gallbladder and Extrahepatic Biliary Disease

Differential Diagnosis

Obstructive Disease

Extrahepatic biliary obstruction
- Pancreatitis (most common etiology in dog)
- Biliary neoplasia
- Cholangitis
- Pancreatic neoplasia

Cholelithiasis/choledocholithiasis
Gallbladder mucocele

Nonobstructive Disease

Cholecystitis
- Bacterial cholecystitis (ascending infection—*Escherichia coli* most common)
- Necrotizing cholecystitis
- Emphysematous cholecystitis (*E. coli, Clostridium perfringens*)

Cholelithiasis/choledocholithiasis (does not always cause obstruction)
Parasites (mainly seen in cats) Tropical climates (seen in cats that eat lizards or toads)
- *Platynosomum fastosum* (a fluke)
- *Amphimerus pseudofelineus*
- *Metorchis conjunctus*
- *Eurytrema procyonis*

Gallbladder infarct

Neoplasia

Biliary cystadenoma
Bile duct carcinoma

Caroli Disease
Dilatation of intrahepatic and extrahepatic bile ducts

Gallbladder Rupture
Necrotizing cholecystitis
Obstruction
Iatrogenic
Blunt abdominal trauma
Gallbladder torsion

Clinical Findings of Gallbladder and Biliary Disease

Clinical Signs
Vomiting
Icterus
Anorexia
Fever
Abdominal pain
Depression
Weight loss
Ascites/bile peritonitis

Clinicopathologic Findings
Hyperbilirubinemia
Elevated alkaline phosphatase (ALP) levels
Elevated gamma glutamyltransferase (GGT) levels
Elevated serum bile acids
Elevated alanine aminotransferase (ALT) levels
Hypercholesterolemia
Stress leukogram
Nonregenerative anemia

Radiographic Findings
Hepatomegaly
Mass effect in area of gallbladder
Gas shadow in area of gallbladder
Choleliths radiopaque if they contain calcium (50% may not be seen on radiographs)

Ultrasonographic Signs
Dilated and tortuous bile ducts
Gallbladder distension
Thickened gallbladder wall
Cholelith visible
Pancreatic mass identified
Stellate appearance to contents of gallbladder (characteristic of a gallbladder mucocele)

Hepatic Encephalopathy

Clinical Findings

General Systemic Clinical Signs

Anorexia
Depression
Weight loss
Lethargy
Nausea
Fever
Ptyalism
Intermittent vomiting
Diarrhea

Central Nervous System Clinical Signs

Tremors
Ataxia
Personality change (often toward aggression)
Dementia
Head pressing
Pacing
Circling
Hysteria
Cortical blindness
Seizures
Coma

Hepatic Lipidosis, Feline

Clinical Findings

Historical Findings

Obesity
Recent anorexia and rapid weight loss

- Concurrent disease that causes anorexia (pancreatitis, diabetes mellitus, inflammatory hepatobiliary disease, inflammatory bowel disease, feline infectious peritonitis, chronic renal failure, neoplasia, cardiomyopathy, neurologic disease, etc.)
- Stressful event
- Abrupt diet change

Typically indoor cats

Physical Findings

Jaundice
Vomiting
Dehydration

Hepatic encephalopathy
- Depression
- Ptyalism

Hepatomegaly

Clinicopathologic Findings

Typical findings of cholestasis
- Moderate increase in alanine aminotransferase (ALT)
- Marked increase in alkaline phosphatase (ALP)
- Mild increase in gamma glutamyltransferase (GGT); disproportionately low compared with other feline cholestatic hepatopathies
- Elevated serum bile acids typical

Coagulation test abnormalities (especially in conjunction with acute pancreatitis)

Cytology (Ultrasound-Guided Needle Aspirates) and Histopathology

Reveal clear vacuolation of most hepatocytes, nonzonal in distribution; typically with absence of inflammatory cells

Hepatobiliary Disease

Clinical and Physical Findings

General Clinical Features

Depression
Anorexia
Lethargy
Weight loss
Poor haircoat, insufficient grooming
Nausea, vomiting
Diarrhea
Dehydration
Small body stature
Polydipsia, polyuria

Signs Specific but Not Pathognomonic for Hepatic Disease

Icterus
Bilirubinuria
Acholic feces
Organomegaly
Ascites
Hepatic encephalopathy
- Behavioral changes (aggression, dementia, hysteria)
- Circling
- Ataxia

- Staggering
- Pacing
- Head pressing
- Cortical blindness
- Ptyalism
- Tremors/seizures
- Coma

Coagulopathies
Polydipsia/polyuria

Causes of Elevated Serum Hepatobiliary Enzymes

Primary Hepatic Disease

Drug Induction
Corticosteroids (dogs)
Anticonvulsants (phenobarbital, phenytoin, primidone)

Endocrinopathies
Hyperadrenocorticism (dogs)
Hypothyroidism (dogs)
Hyperthyroidism (cats)
Diabetes mellitus

Bone Disorders
Growing animals
Osteosarcoma
Osteomyelitis

Neoplasia
Adenocarcinomas (pancreatic, intestinal, adrenocortical, mammary)
Sarcomas (hemangiosarcoma, leiomyosarcoma)
Hepatic metastasis

Muscle Injury
Acute muscle necrosis/trauma
Myopathies
Malignant hyperthermia

Hypoxia/Hypotension
Septic shock
Surgery
Congestive heart failure
Hypoadrenocorticism
Circulatory shock
Severe acute blood loss
Hypotensive crisis
Status epilepticus

Gastrointestinal Disease
Pancreatitis
Inflammatory bowel disease

Miscellaneous Causes
Systemic infections
Pregnancy (cats—increased placental alkaline phosphatase)
Colostrum-fed neonates (dogs)
Breed related (Scottish terrier)

Differential Diagnosis, Dogs

Inflammation
Chronic hepatitis complex
- Copper accumulation—Bedlington Terrier, Airedale Terrier, Bull Terrier, Bulldog, Cocker Spaniel, Collie, Dachshund, Dalmatian, Doberman Pinscher, German Shepherd, Golden Retriever, Keeshond, Kerry Blue Terrier, Labrador Retriever, Norwich Terrier, Old English Sheepdog, Pekingese, Poodle, Samoyed, Schnauzer, Skye Terrier, West Highland White Terrier, Wire Fox Terrier
- Drug induced: trimethoprim-sulfa, phenobarbital, diethylcarbamazine, oxibendazole, many others
- Familial hepatitis—Doberman Pinscher, West Highland White Terrier, Dalmatian, Skye Terrier, Cocker Spaniel

Fibrosis and cirrhosis (results from any severe or chronic hepatic insult)
Infectious agents: leptospirosis, canine adenovirus type 1 infection, bacterial hepatitis, histoplasmosis, Rocky Mountain spotted fever, ehrlichiosis, babesiosis, leishmaniasis
Cholangiohepatitis
Granulomatous hepatitis
- *Rhodococcus, Borrelia, Bartonella, Histoplasma, Coccidioidomyces, Hepatozoon, Heterobilharzia Nocardia, Mycobacterium* spp.

Acidophil cell hepatitis
Lobular dissecting hepatitis
Hepatic abscess

Acute Toxic or Drug-Induced Hepatopathy

Vacuolar Hepatopathy

Metabolic Liver Disease
Amyloidosis
Hyperlipidemia
Lysosomal storage disease

Vascular Hepatic Disease
Congenital portosystemic venous anomaly
Intrahepatic portal vein hypoplasia
Intrahepatic arteriovenous fistula

Biliary Tract Disease

Neoplasia
Primary: hepatocellular carcinoma, hepatocellular adenoma, hepatic hemangiosarcoma, biliary carcinoma
Other hepatic tumors: leiomyosarcoma, liposarcoma, myxosarcoma, fibrosarcoma, biliary adenoma, hepatic carcinoid
Hemolymphatic: lymphosarcoma, mast cell tumor, plasma cell tumor
Metastatic neoplasia

Hepatic or Biliary Cysts

Differential Diagnosis, Cats

Hepatic Lipidosis

Inflammatory Hepatobiliary Disease
Cholangitis/cholangiohepatitis complex
- Suppurative (neutrophilic) cholangitis, cholangiohepatitis
- Lymphocytic cholangitis

Chronic cholangiohepatitis (later stage of acute cholangiohepatitis)
Sclerosing cholangitis
Lymphocytic portal hepatitis
Feline infectious peritonitis (FIP)

Toxic Hepatopathy
Antimicrobials (trimethoprim-sulfa, tetracycline)
Anticonvulsants (phenobarbital)
Diazepam
Methimazole
Griseofulvin
Ketoconazole
Pine oils (cleaning agents)
Amanita phalloides (death cap mushroom)
Natural or herbal remedies
Many others

Portosystemic Venous Anomaly

Lipoprotein Lipase Deficiency

Neoplasia
Primary Hepatic Neoplasia
Biliary carcinoma
Hepatocellular carcinoma

Hepatic hemangiosarcoma
Bilary cystadenoma
Myelolipoma
Hepatic carcinoid

Hemolymphatic Neoplasia

Lymphosarcoma
Mast cell tumor
Plasma cell tumor

Metastatic Neoplasia

Hepatomegaly and Microhepatica

Differential Diagnosis

Generalized Hepatomegaly

Acute toxic hepatopathy
Infiltrative hepatic disease
- Neoplasia: primary or metastatic
- Chronic hepatitis complex (dog)
- Cholangiohepatitis (cat)
- Extramedullary hematopoiesis
- Mononuclear-phagocytic cell hyperplasia
- Amyloidosis (rare)

Passive congestion
- Right-sided heart failure
- Pericardial disease (dog)
- Caval syndrome (dog)
- Caudal vena cava obstruction (dog)
- Budd-Chiari syndrome (rare)

Hepatocellular hypertrophy
- Hepatic lipidosis
- Steroid hepatopathy
- Anticonvulsant drug therapy

Acute extrahepatic bile duct obstruction

Focal Hepatomegaly

Neoplasia: primary or metastatic
Nodular hyperplasia
Chronic hepatic disease with fibrosis and nodular regeneration
Hepatic abscess
Hepatic cyst

Microhepatica

Decreased hepatic mass
- Chronic hepatic disease with progressive loss of hepatocytes

Decreased portal blood flow with hepatocellular atrophy
- Congenital portosystemic shunt
- Intrahepatic portal vein hypoplasia
- Chronic portal vein thrombosis

Hypovolemia
- Hypoadrenocorticism
- Shock

Hyperlipidemia

Differential Diagnosis

Postprandial Hyperlipidemia

Primary

Idiopathic hyperlipoproteinemia of Miniature Schnauzers
Feline familial hyperchylomicronemia
Idiopathic hypercholesterolemia (rare—Doberman Pinscher, Rottweiler)
Idiopathic hypercholesterolemia

Secondary

Endocrine
- Hypothyroidism
- Diabetes mellitus
- Hyperadrenocorticism

Pancreatitis
Nephrotic syndrome
Hepatic insufficiency
Cholestasis
Drug induced
- Glucocorticoids
- Megesterol acetate

Clinical Findings

Severe Hyperlipidemia

Intermittent gastrointestinal signs
- Vomiting
- Diarrhea
- Abdominal discomfort

Seizures
Pancreatitis
Lipemia retinalis
Cutaneous xanthomas
Peripheral nerve paralysis
Behavioral changes

Severe Hypercholesterolemia
- Arcus lipoides corneae
- Lipemia retinalis
- Atherosclerosis

Pancreatitis

Clinical Findings of Acute Pancreatitis

Dogs

Mild Acute Pancreatitis
- Depression
- Anorexia
- Nausea, vomiting, diarrhea
- Ptyalism
- Mild right cranial abdominal pain
- Fever, dehydration, weakness

Moderate to Severe Acute Pancreatitis
- Depression
- Anorexia
- Vomiting
- Right cranial abdominal pain
- Hematemesis, hematochezia, melena
- Jaundice
- Respiratory distress
- Shock, fever, dehydration
- Hyperemic mucous membranes
- Tachycardia, tachypnea
- Abdominal effusion
- Mass effect in region of pancreas
- Petechiae, ecchymoses
- Cardiac arrhythmia
- Glossitis, glossal slough
- Extrahepatic biliary obstruction

Cats
- Signs tend to be more subclinical and nonspecific.
- May be associated with inflammatory bowel disease
- May be component of multisystemic disease such as toxoplasmosis
- Lethargy, anorexia, vomiting, dehydration, weight loss, jaundice, hypothermia
- May present as acute necrotizing or acute suppurative form

Predisposing Factors

Nutritional

Obesity
High-fat diet
After ingestion of large, fatty meal

Hypertriglyceridemia

Hyperlipoproteinemia (Idiopathic in Miniature Schnauzers)
Endocrine (diabetes mellitus, hyperadrenocorticism, hypothyroidism)

Drugs

Chemotherapeutic agents
- L-Asparaginase
- Azathioprine
- Others

Organophosphates
Asparaginase
Thiazides
Furosemide
Estrogens
Sulfa drugs
Procainamide
Potassium bromide
Tetracyclines

Ischemia

Hypovolemia
Associated with disseminated intravascular coagulation (DIC)
Vasoactive amine–induced vasoconstriction
Surgery
Gastric dilatation/volvulus
Severe immune-mediated hemolytic anemia

Duodenal Reflex

Increased intraluminal pressure during severe vomiting

Other

Cholangitis
Infection (toxoplasmosis, feline infectious peritonitis)
Abdominal trauma
Hypercalcemia
Trauma

Clinicopathologic Findings in Dogs and Cats with Acute Pancreatitis

- BUN/creatinine—increased in 50 to 65% of dogs and in 33% (Cr) and 57% (BUN) in cats. Usually prerenal due to dehydration and hypotension. May be secondary to intrinsic renal failure (sepsis and immune-complex)
- Potassium—decreased in 20% of cases in dogs and 56% in cats. Increased loss in vomiting and due to renal loss with fluid therapy plus reduced intake and aldosterone release caused by hypovolemia
- Sodium—can be increased, decreased or normal. Increase usually caused by dehydration, decrease caused by losses secondary to vomiting
- Calcium—Commonly decreased in cats, rarely in dogs, rarely increased in both dogs and cats. Reduction is a poor prognostic indicator in cats but no prognostic significance in dogs. May be caused by saponification in peripancreatic fat and glucagon release stimulating calcitonin
- Chloride—Very commonly decreased in dogs. Loss in gastrointestinal secretions in vomiting
- Phosphate—Often increased in dogs, uncommonly increased or decreased in cats. Increase usually due to reduced renal excretion secondary to renal compromise. Decrease (in cats) due to treatment for diabetes mellitus
- Glucose—increased in 40-88% of dogs and decreased in up to 40%. Increased in 64% of cats, rarely decreased. Increase due to decreased insulin and increased glucagon, cortisol, and catecholamines. Decrease caused by sepsis or anorexia
- Albumin—Increased in 39-50% and decreased in 17% of dogs. Increased in 8-30% and decreased in 40% of cats. Increase due to dehydration. Decrease due to gut loss, malnutrition, concurrent hepatic disease, or renal loss
- Hepatocellular enzymes (ALT, AST)—increased in 61% of dogs and 68% of cats. Hepatic necrosis and vacuolation due to sepsis, local effects of pancreatitis +/– concurrent hepatic disease in cats
- Cholestatic enzymes (ALP and GGT)—Increased in 79% of dogs and 50% of cats. Biliary obstruction due to acute or chronic pancreatitis +/– concurrent cholangitis +/– lipidosis in cats; steroid-induced ALP in dogs
- Bilirubin—Increased in 53% of dogs and 64% of cats (same causes as GGT and ALP)

- Cholesterol—Increased in 48-80% of dogs and 64% of cats. Can be due to cholestasis; unclear if cause or effect
- Triglycerides—Commonly increased in dogs. Unclear if cause or effect
- Neutrophils—Increased in 55-60% of dogs, increased in 30% and decreased in 15% of cats. Increased due to inflammatory response. Decreased in some cats due to consumption, may be a poor prognostic indicator
- Hematocrit—Increased in about 20% and decreased in 20% of both dogs and cats. Increased due to dehydration and decreased due to anemia of chronic disease or gastric ulceration
- Platelets—Commonly decreased in severe cases in dogs. Decreased due to circulating proteases +/– disseminated intravascular coagulation

Portosystemic Shunt, Congenital

Clinical Findings

Signalment

Young animal, male or female, often purebred

History

Neurologic signs (dementia, circling, central blindness, personality change, head pressing, wall hugging, seizures)
Vomiting
Diarrhea
Ptyalism (especially cats)
Worsening of signs after eating
Improvement of signs with antimicrobial therapy
Prolonged recovery from anesthesia
Polydipsia/polyuria
Recurrent urate urolithiasis in breeds other than Dalmatian and English Bulldog

Physical Examination

Poor haircoat
Small stature
Cystic calculi
Cryptorchidism
Bilateral renomegaly
Copper-colored irises in non-Asian cat breeds
Other congenital anomalies

Clinicopathologic Findings

Microcytosis
Hypoalbuminemia
Mild increases in hepatic enzymes
Hypocholesterolemia
Low BUN
Normal to high resting bile acids/elevated postprandial bile acids
Hyposthenuria
Urate crystalluria and urolithiasis

Vacuolar Hepatopathy, Canine

Differential Diagnosis

Hyperadrenocorticism
- Pituitary dependent
- Adrenal dependent
- Iatrogenic (glucocorticoid therapy)

Pancreatitis
- Chronic

Severe hypothyroidism
Chronic stress
- Illness of more than 4 months

Chronic infection or inflammation (e.g., pyelonephritis, chronic dermatitis)
Severe dental disease
- Oral infection

Disorders affecting lipid metabolism
- Diabetes mellitus
- Idiopathic hyperlipidemia

Neoplasia
- Lymphoma

Congestive heart failure
Abnormal sex hormone production
Inflammatory bowel disease
- Chronic, lymphoplasmacytic, eosinophilic

Hepatocutaneous syndrome

SECTION X

Neoplasia

Chemotherapeutic Agent Toxicity

Most severely affects tissues with a growth fraction that approaches that of tumor cells

Clinical Findings

Myelosuppression

Neutropenia: short-lived cells; nadir is 5-10 days postchemotherapy
Thrombocytopenia: nadir is 7-14 days postchemotherapy
Anemia: erythrocytes live longer; rarely clinically significant

Gastrointestinal Toxicity

Nausea, vomiting
Diarrhea
Inappetence
Anorexia

Cardiotoxicity

Doxorubicin therapy
Breeds susceptible to dilated cardiomyopathy (e.g., Doberman) most sensitive
Most likely after cumulative dose of 180 mg/m^2

Nephrotoxicity

Cisplatin, streptozotocin
Limit use of cisplatin in cases of preexisting renal disease.

Hepatopathy

Irreversible hepatic toxicity may result if lomustine (CCNU) given in face of elevated ALT

Urothelial Toxicity
Sterile hemorrhagic cystitis
Cyclophosphamide, ifosfamide

Extravasation
Doxorubicin: severe local reaction leading to slough
Vincristine: usually minor tissue damage

Hypersensitivity
Doxorubicin: caused by histamine release from mast cells; prevented by slow administration
L-Asparaginase: less likely if given subcutaneously rather than intravenously
Etoposide, paclitaxel: caused by carrier solutions for these agents

Alopecia
Less of a problem in dogs and cats than in people
Worse in breeds that have hair (e.g., Poodles, Terriers, Old English Sheepdogs) than in dogs with fur
Loss of "feathers" (e.g., Golden Retrievers)
Loss of whiskers in cats

Neurologic Toxicity
Fatal neurotoxicity in cats with topical or systemic administration of 5-fluorouracil

Respiratory Toxicity
Fatal, acute pulmonary edema in cats with cisplatin therapy

Corticosteroid Therapy

Adverse Effects Associated with Glucocorticoid Administration

Polyuria/polydipsia
Polyphagia
Increased alkaline phosphatase (ALP) levels
Increased gamma glutamyltransferase (GGT) levels
Panting
Insomnia, agitation, behavioral changes
Immunosuppression
- Secondary infection
- Recrudescence of latent infection
- Worsening of existing infection
- Demodicosis

Vacuolar hepatopathy
Iatrogenic hyperadrenocorticism
Adrenocorticoid deficiency with rapid withdrawal after sustained use

Alopecia
Calcinosis cutis
Comedones
Skin thinning
Proteinuria
Muscle atrophy/muscle wasting
Myotonia/myopathy
Delayed wound healing
Colonic perforation
Gastrointestinal ulceration
Insulin resistance
Diabetes mellitus
Hyperlipidemia
Abortion
Growth suppression
Hypercoagulable state
Ligament and tendon rupture
Psychosis/behavior change
Lowered seizure threshold
Osteopenia

Histiocytic Disease

Classification, Dogs

May be difficult to differentiate from lymphoproliferative, granulomatous, or reactive inflammatory disease by histopathology alone

Cutaneous Histiocytoma
Benign, usually solitary lesion
Typically young dogs
Often spontaneously regress

Langerhans Cell Histiocytoma
Rare, rapidly metastatic, cutaneous infiltration by histiocytes, may be limited to multiple cutaneous sites or may affect lymph nodes and internal organs

Cutaneous Histiocytosis
Single or multiple lesions
May spontaneously regress
May respond to immunosuppressive drugs

Systemic Histiocytosis
Familial disease of Bernese Mountain Dogs, rarely other breeds
Similar lesions to cutaneous histiocytosis but may also affect mucous membranes, lymphoid organs, lung, bone marrow, and other organ systems
Progressive, requires immunosuppressive therapy

Histiocytic Sarcoma

Bernese Mountain Dog, Rottweiler, Flat-Coated Retriever, Golden Retriever, rarely other breeds

Histiocytic sarcoma usually begins as a localized lesion in spleen, lymph nodes, lung, bone marrow, skin and subcutis, brain, and periarticular tissue of appendicular joints.

- Rapidly disseminates to multiple organs

Malignant Histiocytosis

Bernese Mountain Dog, Rottweiler, Flat-Coated Retriever, Golden Retriever, rarely other breeds

Multisystemic, rapidly progressive disease of multiple organs

Classification, Cats

Feline Progressive Histiocytosis

Rare, usually see multiple skin nodules, papules, plaques

Head, lower extremities, trunk

Poor long-term prognosis

Feline Histiocytic Sarcoma

Poorly demarcated tumors of subcutis or spleen

Poor prognosis

Humoral Hypercalcemia

Differential Diagnosis

Hematologic Cancers

- Lymphosarcoma
- Lymphocytic leukemia
- Myeloproliferative disease
- Myeloma

Solid Tumors with Bone Metastasis

- Mammary adenocarcinoma
- Nasal adenocarcinoma
- Epithelial-derived tumors
- Pancreatic adenocarcinoma
- Lung carcinoma

Solid Tumors without Bone Metastasis

- Apocrine gland adenocarcinoma of the anal sac
- Interstitial cell tumor
- Squamous cell carcinoma
- Thyroid adenocarcinoma

- Lung carcinoma
- Pancreatic adenocarcinoma
- Fibrosarcoma

Lymphoma

Common Differential Diagnoses

Generalized Lymphadenopathy

Disseminated infections
- Bacterial, fungal, rickettsial, parasitic, viral

Immune-mediated disease
- Systemic lupus erythematosus (SLE), polyarthritis vasculitis, dermatopathy

Other hematopoietic tumors
- Leukemia, multiple myeloma, malignant or systemic histiocytosis

Neoplasia metastatic to lymph nodes
Benign reactive hyperplastic syndromes in cats

Alimentary Disease

Inflammatory bowel diseases
- Lymphocytic/plasmacytic, eosinophilic enteritis

Nonlymphoid intestinal neoplasia
Granulomatous enteritis
Granulated round cell tumors in cats
Gastrointestinal mast cell neoplasia in cats

Cutaneous Disease

Infectious dermatitis (deep pyoderma, fungal dermatitis)
Immune-mediated dermatitis (e.g., pemphigus foliaceus)
Other cutaneous neoplasms

Mediastinal Disease

Thymoma
Chemodectoma (heart base tumor)
Ectopic thyroid neoplasia
Pulmonary lymphomatoid granulomatosis
Granulomatous disease (e.g., hilar lymphadenopathy with blastomycosis)

Paraneoplastic Syndromes

Classification

General

Cancer anorexia, cachexia
Fever

Hematologic

Anemia
- Anemia of chronic disease
- Immune-mediated hemolytic anemia
- Bone marrow infiltration
- Blood loss anemia
- Hyperestrogenism
- Microangiopathic hemolytic anemia

Polycythemia (rare)
- Associated with renal neoplasia, nasal fibrosarcoma, lymphoma, bronchial carcinoma, cecal leiomyosarcoma, transmissible venereal tumor, schwannoma

Leukocytosis
- Neutrophilic
- Eosinophilic

Thrombocytopenia
- Increased consumption
- Decreased production (bone marrow neoplasia)
- Increased destruction (immune-mediated thrombocytopenia)

Thrombocytosis

Thrombocyte hyperaggregability/hypercoagulability

Pancytopenia

Coagulation disorders
- Disseminated intravascular coagulation (DIC)
- Coagulation-activating substances produced by tumor

Hyperproteinemia/hyperglobulinemia

Endocrine

Hypercalcemia of malignancy

Hypoglycemia

Syndrome of inappropriate antidiuretic hormone (ADH) secretion
- Hyponatremia, serum
- Hypoosmolality, urine
- Hyperosmolality

Hyperestrogenism (Sertoli cell tumor)

Gastrointestinal

Gastroduodenal ulceration
- Mast cell tumors, gastrinoma

Cancer cachexia

Renal

Glomerulonephritis

Hypercalcemic nephropathy

Cutaneous

Superficial necrolytic dermatitis
Nodular dermatofibrosis
Feline paraneoplastic alopecia

Neuromuscular

Myasthenia gravis
- Dogs with thymoma

Peripheral neuropathy
- Multiple myeloma, lymphoma, various carcinomas and sarcomas

Hypertrophic Osteodystrophy

Space-occupying mass in thorax or rarely abdomen

Sarcomas

Classification of Soft Tissue Sarcomas

Fibrosarcoma
Mast cell tumor
Undifferentiated sarcoma
Hemangiosarcoma
Hemangiopericytoma (peripheral nerve-sheath tumor)
Myxosarcoma
Leiomyosarcoma
Malignant fibrous histiocytoma
Schwannoma
Neurofibrosarcoma
Synovial cell sarcoma
Rhabdomyosarcoma
Liposarcoma
Vaccine-associated fibrosarcoma (cats)

Clinical Findings for Hemangiosarcoma

Older dogs and cats
Many potential sites of origin
- Spleen
- Right atrium
- Subcutis
- Pericardium
- Liver
- Muscle
- Lung
- Skin
- Bone
- Kidney
- Central nervous system

- Peritoneum
- Oral cavity
- Nasal cavity
- Eye
- Retroperitoneum

Hemoabdomen
Pericardial effusion
Cardiac tamponade
Sudden death
Anorexia, vomiting
Lethargy
Right-sided heart failure
Muffled heart sounds
Arrhythmias
Neurologic signs (may metastasize to brain)

Thyroid Neoplasms

Classification and Clinical Findings

Cats

Hyperthyroidism: functional thyroid tumors

- Thyroid adenoma
- Thyroid adenocarcinoma

Dogs

Nonfunctional Tumors (90%)

Thyroid adenoma
Thyroid adenocarcinoma

- Swelling or mass in neck
- Dyspnea
- Cough
- Lethargy
- Dysphagia
- Regurgitation
- Anorexia
- Weight loss
- Horner syndrome
- Change in bark
- Facial edema

Functional Tumors (10%)

Thyroid adenoma
Thyroid adenocarcinoma

- Swelling or mass in neck
- Polyphagia/weight
- Hyperactivity

- Polyuria/polydipsia
- Panting
- Change in behavior (aggression)

Tumors

Bone and Joint Tumors, Classification

Canine osteosarcoma
- Appendicular
- Skull
- Scapular
- Pelvic
- Ribs
- Vertebral
- Nasal and paranasal

Chondrosarcoma
Fibrosarcoma
Hemangiosarcoma
Multilobular osteochondrosarcoma
Osteoma
Canine multiple cartilaginous exostoses
Feline osteosarcoma
Feline multiple cartilaginous exostoses
Metastatic bone tumors
- Transitional cell carcinoma
- Prostatic adenocarcinoma
- Mammary carcinoma
- Thyroid carcinoma
- Pulmonary carcinoma
- Nasal carcinoma
- Apocrine gland, anal sac adenocarcinoma
- Renal tumors
- Others

Primary joint tumors
- Synovial cell sarcoma
- Histiocytic sarcoma
- Malignant fibrous histiocytoma
- Synovial myxoma
- Myxosarcoma
- Osteosarcoma
- Fibrosarcoma
- Chondrosarcoma
- Hemangiosarcoma
- Liposarcoma
- Rhabdomyosarcoma
- Undifferentiated sarcoma

Hematopoietic Tumors, Classification

Lymphoma

Feline

- Alimentary
- Multicentric
- Mediastinal/thymic
- Nasal
- Renal
- Other
- Feline leukemia virus (FeLV) associated

Canine

- Multicentric
- Others (alimentary, mediastinal, cutaneous)

Lymphoid Leukemia

- Acute lymphoblastic leukemia (in cats, often associated with FeLV infection)
- Chronic lymphocytic leukemia

Nonlymphoid Leukemias and Myeloproliferative Disorders

- Acute myelogenous leukemia (myeloblastic)
- Acute myelomonocytic leukemia (myeloblasts/monoblasts)
- Acute monocytic leukemia (monoblasts)
- Acute megakaryoblastic leukemia (megakaryoblasts)
- Erythroleukemia (erythroblasts)

Chronic Myeloproliferative Disorders

- Chronic myelogenous leukemia (neutrophils, late precursors)
- Primary thrombocythemia (platelets)
- Basophilic leukemia (basophils and precursors)
- Eosinophic leukemia (eosinophils and precursors)
- Polycythemia vera (erythrocytes)

Plasma Cell Neoplasms

- Multiple myeloma
- Solitary plasmacytoma
- IgM (Waldenström macroglobulinemia)

Mast Cell Tumor (MCT) Disease, Clinical Findings

Clinical Appearance and Location of MCTs

- Extremely variable in appearance
- Soft, fluctuant, firm, discrete, diffuse, small, large, solitary, multiple, haired, hairless, dermal, or subcutaneous
- Erythema, bruising, ulceration

On trunk most often; also perineum, extremities, head, neck
Rarely oral cavity, nasal cavity, larynx, conjunctiva

Systemic Signs of Disseminated Mastocytosis

Gastrointestinal ulceration
Abdominal discomfort
Vomiting
Melena
Hypotension
Coagulation abnormalities
Acute or chronic blood loss anemia

Oral Cavity Tumors, Differential Diagnosis

Malignant Neoplasms

Melanoma
Squamous cell carcinoma
Fibrosarcoma
Osteosarcoma
Lingual carcinoma or sarcoma
Histiocytic sarcoma
Lymphoma
Mast cell tumor

Benign Neoplasms

Epulides (acanthomatous ameloblastoma)
- Fibromatous
- Ossifying
- Acanthomatous (squamous): may be invasive but does not metastasize

Papillomas: self-limiting
Fibroma
Lipoma
Chondroma
Osteoma
Odontoma
Cementoma
Plasmacytoma
Hemangioma
Hemangiopericytoma
Histiocytoma
Eosinophilic granuloma

Skin and Subcutaneous Tumors

Epithelial Tumors

Sebaceous gland adenoma/adenocarcinoma
Squamous cell carcinoma

- Canine cutaneous squamous cell carcinoma
- Canine nasal planum squamous cell carcinoma
- Canine digital squamous cell carcinoma
- Feline cutaneous squamous cell carcinoma
- Feline multicentric squamous cell carcinoma in situ (Bowen disease)

Trichoepithelioma
Intracutaneous cornifying epithelioma
Basal cell tumors
- Benign tumors
- Basal carcinoma

Trichoblastoma
Pilomatricoma
Papilloma
Perianal gland tumors (hepatoid gland tumors)
Sweat gland tumors (apocrine gland tumors)
Ceruminous gland tumors
Anal sac, apocrine gland tumors
Follicular stem cell carcinoma

Round Cell Tumors

Lymphoma
Mast cell tumor
Histiocytoma
Transmissible venereal tumor (TVT)
Plasmacytoma

Melanocytic Tumors

Melanoma
- Benign (typically melanomas of haired skin and eyelids)
- Malignant (typically those of digit or mucocutaneous junctions)

Urogenital Tumors, Classification

Kidney

Lymphoma (most common renal tumor in cats)
Primary renal carcinoma, adenoma/adenocarcinoma
Cystadenocarcinoma with concurrent nodular dermatofibrosis in German Shepherds
Tumors of embryonic origin (e.g., Wilm tumor)
Nephroblastoma
Transitional cell carcinoma

Urinary Bladder

Older female dogs, West Highland White Terrier, Scottish Terriers, Beagles, Dachshunds, Shetland Sheepdogs
Transitional cell carcinoma

Squamous cell carcinoma
Leiomyosarcoma
Leiomyoma
Rhabdomyosarcoma
Metastatic neoplasia
- Hemangiosarcoma
- Lymphoma
- Extension of prostate neoplasia

Prostate
Prostatic adenocarcinoma
Transitional cell carcinoma

Penis and Prepuce
Prepuce affected by tumors of haired skin seen elsewhere
Penile
- Transmissible venereal tumor
- Others

Testicular Neoplasia
Cryptorchid dogs are 13.6 times more likely to develop Sertoli cell tumor or seminoma
Sertoli cell tumor (25-50% are functional and cause hyperestrogenemia)
Leydig cell (interstitial) tumor
Seminoma

Vagina and Vulva
Leiomyoma
Fibroleiomyoma
Fibroma
Polyps
Lipoma
Leiomyosarcoma (rare)
Transmissible venereal tumor (TVT)

Uterus
Leiomyoma
Leiomyosarcoma
Uterine adenocarcinoma

Ovary
Epithelial Tumors (50% of ovarian tumors)
Papillary adenoma
Cystadenoma
Papillary adenocarcinoma
Undifferentiated adenocarcinoma

Germ Cell Tumors (10% of ovarian tumors)
- Dysgerminoma
- Teratoma
- Teratocarcinoma

Sex-Cord Stromal Tumors (40% of ovarian tumors)
- Granulosa cell tumor
- Benign thecoma
- Benign luteoma

Mammary Gland
- Fibroadenoma (mixed mammary tumor)
- Solid carcinomas
- Tubular adenocarcinoma
- Sarcoma
- Inflammatory carcinomas
- Feline mammary adenocarcinomas

SECTION XI

Neurologic and Neuromuscular Disorders

Brain Disease, Congenital or Hereditary

Differential Diagnosis

Congenital Malformations

Failure of normal closure of neural tube: vary in severity from clinically inapparent (agenesis of corpus callosum) to severe (anencephaly)

Lissencephaly: failure of normal migration of neurons in development of cerebral cortex; leads to abnormal appearance of sulci and gyri (most often seen in Lhasa Apso)

Cerebellar hypoplasia: seen most often in cats after in utero panleukopenia infection; rarely seen with parvovirus infection of developing cerebellum in dogs; may be isolated malformation without infection

Chiari-like malformations: protrusion of cerebellar vermis through foramen magnum (Cavalier King Charles Spaniel, other dog breeds)

Hydrocephalus: congenital hydrocephalus seen most often in toy and brachycephalic breeds; suggests hereditary basis; often congenital stenosis or aplasia of mesencephalic aqueducts

Inborn errors of metabolism (hereditary): young, purebred animals with diffuse, symmetric signs of brain disease
- Organic acidurias
- Spongiform encephalopathies: may be hereditary or acquired (transmissible) disease
- Polioencephalopathies: metabolic defects that affect gray matter
- Neuroaxonal dystrophy: spheroids causing swelling within axons
- Leukoencephalopathies: disorders of myelin; affect white matter; often affect cerebellum and long tracts leading to tremors and dysmetria
- Lysosomal storage diseases: accumulation of metabolic products in lysosomes
- Ceroid lipofuscinosis: accumulation of proteins in lysosomes
- Neonatal encephalopathy: hereditary disease of Standard Poodles

Movement Disorders

Hereditary cerebellar hypoplasia
Multisystem degeneration: diseases of cerebellum and basal ganglia—progressive neuronal abiotrophy of Kerry Blue Terriers and Chinese Crested dogs
Dyskinesis and dystonias
Paroxysmal dyskinesias ("Scotty cramp" or idiopathic cerebellitis)—Scottish Terriers

Cognitive Dysfunction

Clinical Findings

Disorientation
Sleep/wake cycle alterations
House soiling problems
Change in activity levels
- Increased
- Stereotypic
- Decreased

Agitation
Anxiety
Altered responsiveness to stimuli
- Heightened
- Reduced

Changes in appetite
- Increased
- Decreased

Decreased ability to perform learned tasks
Changes in interaction with owners

Cranial Nerve (CN) Deficits

Clinical Findings

CN I (Olfactory)
Loss of ability to smell

CN II (Optic)
Loss of vision, loss of menace response, dilated pupil, loss of papillary light reflex (direct and consensual)

CN III (Oculomotor)
Loss of papillary light reflex on affected side (even if light shone in opposite eye), dilated pupil, ptosis, ventrolateral strabismus

CN IV (Trochlear)
Slight dorsomedial eye rotation

CN V (Trigeminal)
Atrophy of temporalis and masseter muscles, loss of jaw tone and strength, dropped jaw (if bilateral), analgesia of innervated areas

CN VI (Abducens)
Medial strabismus, impaired lateral gaze, poor retraction of globe

CN VII (Facial)
Lip, eyelid, and ear droop; loss of ability to blink; loss of ability to retract lip; possibly decreased tear production

CN VIII (Vestibulocochlear)
Ataxia, head tilt, nystagmus, deafness, positional strabismus

CN IX (Glossopharyngeal)
Loss of gag reflex, dysphagia

CN X (Vagus)
Loss of gag reflex, laryngeal paralysis, dysphagia, megaesophagus

CN XI (Accessory)
Atrophy of trapezius, sternocephalicus, and brachiocephalicus muscles

CN XII (Hypoglossal)
Loss of tongue strength, inability to retract tongue if bilateral, atrophy of tongue

Head Tilt

Differential Diagnosis

Peripheral Vestibular Disease

Otitis media/interna
Feline idiopathic vestibular disease
Geriatric canine vestibular disease
Feline nasopharyngeal polyps
Middle ear tumor
- Ceruminous gland adenocarcinoma
- Squamous cell carcinoma

Trauma
Aminoglycoside ototoxicity/chemical ototoxicity
Hypothyroidism (possibly)

Central Vestibular Disease

Trauma/hemorrhage
Infectious inflammatory disease
- Rocky Mountain spotted fever
- Feline infectious peritonitis (FIP)
- Others

Granulomatous meningoencephalitis
Neoplasia
Vascular infarct
Thiamine deficiency
Metronidazole toxicity

Inflammatory Disease of the Nervous System

Differential Diagnosis

Steroid-responsive meningitis-arteritis (steroid-responsive suppurative meningitis) (juvenile to young adult large breed dogs: Bernese Mountain Dogs, Boxers, German Shorthaired Pointers, Nova Scotia Duck Tolling Retrievers)

Granulomatous meningoencephalitis
- Idiopathic inflammatory brain disease of dogs
- Most commonly in small breed dogs

Pug meningoencephalitis
- Necrotizing meningoencephalitis of cerebral cortex
- Maltese and Yorkshire terrier also

Feline polioencephalomyelitis
- Young cats, progressive course

Feline immunodeficiency virus (FIV) encephalopathy

Bacterial meningitis and myelitis
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*

- *Staphylococcus albus*
- *Pasteurella multocida*
- *Actinomyces*
- *Nocardia*
- Others

Canine distemper virus
Rabies
Feline infectious peritonitis (FIP)
Toxoplasmosis
Neosporosis
Borreliosis
Mycotic infections

- *Cryptococcus neoformans, C. gattii*
- Other disseminated systemic mycoses

Rickettsial diseases

- Rocky Mountain spotted fever
- Ehrlichiosis
- *Ehrlichia ewingii, Anaplasma phagocytophilia*

Parasitic meningitis, myelitis, encephalitis

- Aberrant parasite migration

Intracranial Neoplasms

Differential Diagnosis

Meningioma
Benign tumor of cells of meninges

Neuroepithelial Tumors (Gliomas)
Astrocytomas
Oligodendrogliomas
Choroid plexus tumors (choroid plexus papilloma, ependymal tumor)

Central Nervous System (CNS) Lymphoma
Primary: neoplasia of native CNS lymphocytes
Secondary: metastasis of systemic lymphoma

Metastatic Neoplasia to CNS
Local invasion: nasal adenocarcinoma
Hematogenous spread: melanoma, hemangiosarcoma, lymphosarcoma
Many other neoplasms may metastasize to CNS.

Pituitary Tumors
Functional tumors of pars distalis or pars intermedius: cause pituitary-dependent hyperadrenocorticism; generally cause little damage to surrounding tissue
Pituitary macrotumor

Myasthenia Gravis

Congenital myasthenia gravis: inherited deficiency of acetylcholine receptors at presynaptic membranes of skeletal muscle.

Acquired myasthenia gravis: antibodies made against nicotinic acetylcholine receptors of skeletal muscle.

Clinical Findings

Appendicular muscle weakness
- Worsens with exercise
- Improves with rest
- Tetraplegia

Mentation, postural reactions, reflexes normal

Megaesophagus
- Salivation
- Regurgitation

Dysphagia

Ventroflexion

Urinary bladder distension

Hoarse bark or meow

Persistently dilated pupils

Facial muscle weakness

Aspiration pneumonia

Respiratory weakness

Myositis and Myopathies

Differential Diagnosis

Inflammatory Myopathies

Masticatory myositis
- Immunoglobulin G (IgG) antibodies to type 2M myofibers
- German Shepherd, retrievers, and Doberman Pinscher predisposed
- Young to middle-aged dogs

Canine idiopathic polymyositis
- Large-breed dogs predisposed

Feline idiopathic polymyositis

Dermatomyositis
- Herding breeds, especially Shetland Sheepdog and Collie

Protozoal myositis
- *Toxoplasma gondii*
- *Neospora caninum Hepatozoon, Babesia, Leishmania,* or *Trypanosoma* infection

Bacterial myositis *Clostridium, Leptospira, Ehrlichia,* Rocky Mountain spotted fever
Extraocular myositis (dogs)
Feline immunodeficiency virus

Metabolic Myopathies

Glucocorticoid excess
- Hyperadrenocorticism
- Exogenous corticosteroids

Hypothyroidism
Hypoadrenocorticism
Hypokalemic polymyopathy (cat)
- Increased urinary excretion
- Decreased dietary intake

Mitochondrial myopathies
Lipid storage myopathies
Glycogen storage disorders
Malignant hyperthermia
Hyperkalemic periodic paralysis (American Pit Bull Terrier)

Inherited Myopathies

Muscular dystrophy
- Hereditary Labrador Retriever muscular dystrophy
- Also German Shorthaired Pointer, Rottweiler, others
- Maine Coon, Siamese, Devon Rex, Sphynx, others

Myotonia
- Chow Chow, Staffordshire Bull Terrier, Labrador Retriever, Rhodesian Ridgeback, Great Dane, others

Malignant hyperthermia
- Hypermetabolic disorder of skeletal muscle
- Genetic defect in intracellular calcium homeostasis

Inherited myopathy of Great Danes
Centronuclear myopathy
- Labrador Retriever

Episodic/Exercise-induced collapse
- Labrador Retriever

Exertional rhabdomyolysis

Neurologic Examination

Components

Mental State

Normal
Depression
Stupor
Coma
Agitation
Delirium

Posture
- Normal, upright
- Head tilt
- Wide-based stance
- Recumbent
- Extensor posturing
- Opisthotonus
- Pleurothotonus

Gait
- Proprioceptive deficits
- Paresis
- Circling
- Ataxia
- Dysmetria
- Lameness

Postural Reactions
- Conscious proprioception
- Hopping
- Wheelbarrowing
- Hemiwalking
- Extensor postural thrust

Muscle Tone
- Atrophy
- Decreased muscle tone (lesions of lower motor neurons)
- Increased muscle tone (lesions of upper motor neurons)
- Schiff-Sherrington posture (increased muscle tone and hyperextension of thoracic limbs)

Spinal Reflexes
- Absent, depressed, normal, or exaggerated
- Thoracic limb withdrawal (sixth cervical [C6], C7, C8, first thoracic [T1])
- Biceps (C6-C8) and Triceps (C7-T2) reflexes
- Patellar (fourth lumbar [L4], L5, L6)
- Pelvic limb withdrawal (L6, L7, first sacral [S1])
- Sciatic (L6, L7, S1)
- Cranial tibial (L6, L7)
- Perineal (S1, S2, S3, pudendal nerve)
- Bulbourethral (S1, S2, S3, pudendal nerve)
- Panniculus (response absent caudal to spinal cord lesion, used at T3-L3)
- Crossed extensor reflex (indicative of UMN disease)
- Cutaneous trunci reflex

Sensation and Pain
- Superficial pain
- Deep pain
- Hyperesthesia

Urinary Tract Function

Cranial Nerves

Paroxysmal Disorders Confused with Epileptic Seizures

Differential Diagnosis

Syncope (reduced cerebral blood flow)
- Cardiac arrhythmias
- Hypotension

Episodic Weakness
- Hypoglycemia
- Low blood cortisol
- Electrolyte disturbances

Myasthenia Gravis

Acute Vestibular "Attacks"

Movement Disorders
- Episodic falling
- Scotty cramp
- Head bobbing
- Dyskinesias

Sleep Disorders
- Narcolepsy
- Cataplexy

Obsessive Compulsive Disorder

Peripheral Neuropathies

Clinical signs depend on the nerve affected and the severity of the lesion.

Differential Diagnosis

Focal Disease

Trauma
- Mechanical blows
- Fractures
- Pressure
- Stretching

Laceration
Injection of agents into nerves

Peripheral Nerve Tumors
Schwannoma
Neurofibroma
Neurofibrosarcoma
Lymphoma

Facial Nerve Paralysis
Otitis media
Trauma
Neoplasia
Foreign body (e.g., grass awn)
Nasopharyngeal polyp in cats
Hypothyroidism
Idiopathic

Trigeminal Nerve Paralysis
Bilateral, idiopathic disorder, often self-limiting
Middle-aged to older dogs, rarely cats

Idiopathic Peripheral Vestibular Disease

Hyperchylomicronemia
Leads to xanthomas in skin
May compress peripheral nerves

Ischemic Neuromyopathy
Caudal aortic thromboembolism

Generalized Chronic Polyneuropathies
Idiopathic
Metabolic disorders
- Diabetes mellitus
- Hypothyroidism

Paraneoplastic syndromes
- Insulinoma
- Other tumors

Systemic lupus erythematosus (SLE) or other immune-mediated disease
Chronic organophosphate toxicity
Ehrlichiosis

Generalized Acute Neuropathies
Acute polyradiculoneuritis (“coonhound paralysis”)
Neospora polyradiculoneuritis (puppies)
Disorders of neuromuscular junction
- Botulism
- Tick paralysis
- Myasthenia gravis

Protozoal polyradiculoneuritis
Dysautonomia

Developmental/Congenital Neuropathies

Loss of motor neurons—Cairn Terrier, German Shepherd, English Pointer, Rottweiler, Swedish Lapland, Brittany Spaniel
Loss of peripheral axons—German Shepherd, Alaskan Malamute, Birman cat, Rottweiler, Boxer, Dalmatian
Schwann cell dysfunction—Golden Retriever, Tibetan Mastiff
Loss of sensory neuron of axon and laryngeal nerves—Dachshund, English Pointer, Shorthaired Pointer, Bouvier des Flandres, Siberian Husky
Inborn errors of metabolism

- Hyperchylomicronemia (cat)
- Hyperoxaluria type 2 (shorthaired cat)
- α-L-Fucosidosis (English Springer Spaniel)
- Atypical GM2 gangliosidosis (cat)
- Globoid cell leukodystrophy
- Niemann-Pick disease (Siamese)
- Glycogen storage disease (Norwegian forest cat)

Spinal Cord Disease

Differential Diagnosis

Acute

Trauma
Hemorrhage/coagulopathy
Infarction
Type I intervertebral disk herniation
Fibrocartilaginous embolism
Atlantoaxial subluxation

Subacute/Progressive

Discospondylitis
Noninfectious inflammatory diseases

- Corticosteroid-responsive meningitis/arteritis
- Granulomatous meningoencephalitis
- Feline polioencephalomyelitis

Infectious inflammatory diseases

- Bacterial, fungal, rickettsial, protothecal, protozoal, nematodiasis

Distemper myelitis
Feline infectious peritonitis (FIP) meningitis/myelitis

Chronic Progressive
- Neoplasia
- Type II intervertebral disk protrusion
- Degenerative myelopathy
- Cauda equina syndrome
- Cervical vertebral malformation/malarticulation (wobbler syndrome)
- Lumbosacral vertebral canal stenosis
- Spondylosis deformans
- Hypervitaminosis A (cats)
- Dural ossification
- Diffuse idiopathic skeletal hyperostosis
- Synovial cyst

Progressive in Young Animals
- Neuronal abiotrophies and degenerations
- Metabolic storage diseases
- Atlantoaxial luxation
- Congenital vertebral anomalies

Congenital (Constant)
- Spinal bifida
- Congenital dysgenesis of Manx cats
- Spinal dysraphism
- Hereditary ataxia
- Pilonidal, epidermoid, and dermoid cysts
- Syringomyelia/hydromyelia

Spinal Cord Lesions

Localization

Cranial Cervical Lesion (C1-C5)
- Upper motor neuron (UMN) signs in rear limbs
- UMN signs in forelimbs

Caudal Cervical Lesion (C6-T2)
- UMN signs in rear limbs
- Lower motor neuron (LMN) signs in forelimbs

Thoracolumbar Lesion (T3-L3)
- UMN signs in rear limbs
- Normal forelimbs

Lumbosacral Lesion (L4-S3)
- LMN signs in rear limbs
- Loss of perineal sensation and reflexes
- Normal forelimbs

Sacral Lesion (S1-S3)
- Normal forelimbs
- Normal patellar reflexes
- Loss of sciatic function
- Loss of perineal sensation and reflexes

Systemic Disease

Neurologic Manifestations

Oxygen Deprivation

Vascular Disease

Ischemia
- Thromboembolic disease
- Shock
- Cardiac disease

Hemorrhage (anemia)
- Vessel rupture secondary to hypertension
- Coagulopathy
- Vasculitis

Anesthetic Accidents
- Hypotension
- Cardiac arrhythmia
- Extensive blood loss
- Hypercapnia
- Hypoxemia

Hypoxia
- Pulmonary disease
- Decreased oxygen transport
- Heart failure

Hypertension

Hypoglycemia

Decreased Output or Metabolism
- Primary liver disease
- Malnutrition
- Thiamine deficiency

Increased Uptake

Hyperinsulinemia
- Islet cell tumors
- Insulin overdose

Non–Islet Cell Neoplasia
- Hepatoma
- Leiomyoma

Excessive Metabolism
Sepsis
Breed or activity-related

Increased Uptake of Amino Acids by Extrahepatic Tissues

Water and Ionic Imbalances

Water

Hypoosmolar States (Retention of Free Water)
Hyponatremia

Hyperosmolar States (Loss of Free Water)
Hypernatremia (diabetes insipidus)
Hyperglycemia (diabetes mellitus)

Ions (Excess or Deficiency)

Calcium
Potassium

Endogenous Neurotoxins

Renal Toxins

Hepatoencephalopathy

Endocrine Disease

Adrenal
Hyperadrenocorticism
Hypoadrenocorticism

Adrenergic Dysregulation
Pheochromocytoma

Thyroid
Hypothyroidism
- Myxedema
- Neuromyopathy

Thyrotoxicosis
- Hyperthyroidism
- Iatrogenic

Exogenous Neurotoxins

Plant toxins
Sedative depressant drugs (e.g., antiepileptic drugs)
Heat stroke

Remote Neurologic Manifestations of Cancer

Metastasis to the nervous system
Vascular accidents and infection
Adverse effects of therapy
Paraneoplastic syndromes

Vestibular Disease

Clinical Findings

Central and Peripheral Vestibular Disease

- Head tilt to side of lesion
- Circling/falling/rolling to side of lesion
- Vomiting, salivation
- Incoordination
- Ventral strabismus on side of lesion (±)
- Nystagmus, fast phase away from lesion
- Nystagmus may intensify with changes in body position.

Peripheral Vestibular Disease

- Nystagmus is horizontal or rotatory.
- No change in nystagmus direction with changes in head position
- Postural reactions and proprioception normal
- Concurrent Horner syndrome, cranial nerve VII paralysis with middle/inner ear involvement; other cranial nerves normal

Central Vestibular Disease

- Nystagmus horizontal, rotatory, or vertical
- Nystagmus direction may change direction with change in head position.
- Abnormal postural reactions and proprioception may be seen on side of lesion.
- Multiple cranial nerve deficits may be seen.

Paradoxical Vestibular Syndrome (Cerebellar Lesion)

- Head tilt and circling away from side of lesion
- Fast phase nystagmus toward the lesion
- May exhibit vertical nystagmus
- Abnormal postural reactions on side of lesion
- ± Multiple cranial nerve deficits on side of lesion
- ± Hypermetria, truncal sway, and head tremor

SECTION XII

Ocular Disorders

Anisocoria

Differential Diagonosis

Nonneurologic Causes of Anisocoria

Conditions That Cause Miosis

- Anterior uveitis
- Corneal ulcers and lacerations (reflex miosis mediated by trigeminal nerve)

Conditions That Cause Mydriasis

- Iris atrophy
- Iris hypoplasia
- Glaucoma
- Iridal tumors (e.g., melanoma) that infiltrate iridal musculature
- Unilateral retinal disease (e.g., retinal detachment)
- Severe chorioretinitis that affects a larger area on one eye than the other
- Unilateral optic neuritis or optic nerve neoplasia
- Orbital neoplasia, retrobulbar abscess, cellulitis

Pharmacologic Causes of Anisocoria

Drugs That Cause Miosis (usually agents used for management of glaucoma)

- Pilocarpine
- Demecarium bromide
- Synthetic prostaglandins such as latanoprost

Drugs That Cause Mydriasis

- Tropicamide, atropine

- Ocular contact with toxins like jimsonweed *(Datura stramonium)*
- Ocular decongestants like phenylephrine

Neurologic Causes of Anisocoria

Afferent Lesions

Anisocoria is reduced or abolished in darkness as both pupils dilate. This is because the stimulus producing the anisocoria, light causing constriction of the normal pupil, is eliminated.

- Unilateral retinal or prechiasmal optic nerve lesion
- Unilateral optic tract lesion
- Optic chiasm lesion

Efferent Lesions

Parasympathetic efferent lesions (In dogs, preganglionic efferent nerves are purely parasympathetic and postganglionic nerves are mixed. In cats both nerves are purely parasympathetic.)

- Lesions of the nucleus of CN III, the preganglionic fibers, or the ganglion itself

Sympathetic efferent lesions (Loss of sympathetic tone to the eye is known as Horner syndrome, is always ipsilateral to lesion, and features miosis, ptosis, protrusion of the third eyelid, and enophthalmos.)

- Head, neck, or chest trauma
- Brachial plexus avulsion
- Intracranial, mediastinal, or intrathoracic neoplasia
- Otitis media/interna
- Injury to the ear during ear flushing
- Idiopathic (Golden Retriever and Collie may be predisposed.)

Blindness, Acute

Differential Diagnosis, Dogs and Cats

Cornea

Edema (glaucoma, trauma, endothelial dystrophy, immune-mediated keratitis, neurotropic keratitis, anterior uveitis)
Melanin (entropion, ectropion, lagophthalmos, facial nerve paralysis, keratoconjunctivitis sicca, pannus)
Cellular infiltrate (bacterial, viral, fungal)
Vascular invasion (exposure keratitis)
Fibrosis (scar formation)

Dystrophy (lipid, genetic)
Symblepharon (conjunctiva adhered to cornea)

Aqueous Humor
Fibrin (anterior uveitis: many etiologies)
Hyphema (trauma, coagulopathies, neoplasia, systemic hypertension, retinal detachment)
Hypopyon (immune-mediated, lymphoma, systemic fungal infection, toxoplasmosis, FIP, protothecosis, brucellosis, bacterial septicemia)
Lipemic (hyperlipidemia with concurrent blood-aqueous barrier disruption [uveitis])

Lens
Cataracts (genetic, diabetes, retinal degeneration, hypocalcemia, electric shock, chronic uveitis, lens luxation, metabolic, toxic, traumatic, nutritional)

Vitreous
Hemorrhage (trauma, systemic hypertension, retinal detachment, neoplasia, coagulopathy)
Hyalitis (numerous infectious agents, penetrating injury)

Retina
Retinopathy (glaucoma, sudden acquired retinal degeneration [SARD], progressive retinal atrophy, central progressive retinal atrophy, feline central retinal atrophy, toxicity, taurine deficiency in cats, vitamin E deficiency in dogs, enrofloxacin toxicity in cats)
Chorioretinitis (systemic mycoses, ehrlichiosis, RMSF, canine distemper, toxoplasmosis, FIP, protothecosis, brucellosis, bacterial septicemia, intraocular larval migrans, neoplasia)
Retinal detachment (neoplasia, retinal dysplasia, hereditary/congenital, exudative/transudative disorders such as systemic hypertension or infection-induced inflammatory disease)

Lesions that Prevent Transmission of the Image (optic nerve disease)
Viruses (canine distemper, feline infectious peritonitis [FIP])
Systemic diseases (neoplasia, traumatic avulsion of optic nerve, granulomatous meningoencephalitis, hydrocephalus, optic nerve hypoplasia, immune-mediated optic neuritis, systemic mycoses)

Lesions that Prevent Interpretation of the Visual Message
Canine distemper, FIP, toxoplasmosis, granulomatous meningoencephalitis, systemic mycoses, trauma, heat stroke, hypoxia, hydrocephalus, hepatoencephalopathy, neoplasia, storage diseases, postictal, meningitis

Corneal Color Changes

Diagnostic Tests

Red (blood vessels)
- Mechanism is chronic irritation
- Fluorescein stain, Schirmer tear test (STT), palpebral and corneal reflexes

"Fluffy" Blue (stromal edema)
- Mechanisms are endothelial or epithelial dysfunction
- Fluorescein stain, intraocular pressure (IOP), flare, check for lens luxation

"Wispy" Gray (stromal scar)
- Mechanism is previous (inactive) inflammation
- Fluorescein stain

"Sparkly" White (lipid/mineral accumulation)
- Mechanisms are dystrophy, degeneration, or hyperlipidemia
- Flourescein stain, systemic lipid analysis

Black (pigmentation)
- Mechanism is chronic irritation
- Fluorescein stain, STT

"Punctate" Tan (keratinic precipitates or staphyloma)
- Mechanism is uveitis
- IOP, flare, systemic disease testing

Yellow-Green (inflammatory cell infiltration)
- Inflammation (usually septic)
- Fluorescein stain, cytology, culture and sensitivity testing, polymerase chain reaction (PCR)

Eyelids and Periocular Skin

Differential Diagnosis

Infectious Blepharitis

Bacterial Blepharitis
- Usually *Staphylococcus* spp.
- External hordeolum or stye—infection of the glands of Zeis or Moll
- Internal hordeolum—infection of the meibomian glands
- Chalazion—meibomian secretions thicken and obstruct the duct, leading to glandular rupture and lipogranuloma formation

Fungal Blepharitis

- Dermatophytes *(Microsporum canis, Microsporum gypseum, Trichophyton mentagrophytes)*
- *Malassezia pachydermatitis*—most dogs with *Malassezia* dermatitis have concurrent dermatoses, in cats *Malassezia* infection is linked to systemic disease like diabetes, retroviral infection, internal neoplasia

Parasitic Blepharitis

- Demodecosis
- Feline herpetic ulcerative dermatitis

Allergic Blepharitis

- Atopic dermatitis
- Cutaneous adverse food reaction (food allergy)

Metabolic/Nutritional Blepharitis

- Zinc-responsive dermatosis
- Superficial necrolytic dermatitis (hepatocutaneous disease)

Immune-Mediated Blepharitis

- Pemphigus foliaceus
- Pemphigus erythematosus
- Systemic lupus erythematosus
- Erythema multiforme

Iatrogenic Blepharitis

- Adverse reactions to topical medications

Pigmentary Changes Involving the Eyelid

- Lentigo simplex of orange cats (black macules, not pathogenic)
- Vitiligo (hypopigmentation)
- Uveodermatologic (Vogt-Koyanagi-Harada-like) syndrome (leukoderma)

Neoplastic Blepharitis

- Meibomian gland adenoma
- Papillomas
- Squamous cell carcinoma
- Lymphosarcoma
- Mast cell tumor

Miscellaneous Eyelid Diseases

- Juvenile sterile granulomatous dermatitis and lymphadenitis/juvenile cellulitis (puppy strangles)
- Canine reactive histiocytosis

- Entropion
- Ectropion
- Distichiasis
- Trichiasis

Nonhealing Corneal Erosions (Ulcers) in Dogs

Causes

Establish underlying cause of impaired wound healing.

- Mechanical trauma from lid masses
- Entropion
- Foreign bodies
- Secondary infection
- Corneal exposure caused by lid paralysis
- Exophthalmos
- Buphthalmos
- Tear film abnormalities
- Conformational abnormalities resulting in lagophthalmos
- Corneal edema
- Distichiasis
- Facial fold irritation of cornea

Spontaneous Chronic Corneal Epithelial Defects (SCCEDs)—also called *indolent erosions/ulcers* or *boxer erosions/ulcers*

- Middle-aged dogs
- Boxers predisposed
- Likely instigated by superficial trauma
- Dogs with diabetes mellitus predisposed
- Rim of loose epithelium surrounds corneal defect
- No loss of stromal substance (stromal loss indicates more severe process, typically infection)
- Blepharospasm/epiphora
- Neovascularization may be delayed compared with healing corneal ulcers.

Bullous Keratopathy

Ocular Manifestations of Systemic Diseases

Surface Ocular Disease

Eyelids

Immunosuppressive disorders may predispose to meibomian gland infection with *Demodex* or *Staphylococcus* spp.

Eyelids have mucocutaneous junction; affected by autoimmune disorders such as systemic lupus

erythematosus (SLE) and pemphigoid diseases; also may be affected by uveodermatologic syndrome and vasculitis
Altered lid position, cranial nerve III or VII dysfunction
Horner syndrome: decreased sympathetic tone causing enophthalmos with third eyelid protrusion, ptosis, and miosis; often idiopathic; may be seen with disease of brain, spinal cord, brachial plexus, thorax, mediastinum, neck, temporal bone, tympanic bulla, or orbit

Conjunctivitis

May reflect disease of deeper ocular structures
Good location to detect pallor, cyanosis, icterus
Feline herpesvirus type 1 (FHV-1) and *Chlamydophila felis* are primary pathogens of the conjunctiva.

Cornea/Sclera

Creamy pink discoloration of cornea may be seen with lymphoma.
Corneal lipidosis appears similar; it may be secondary to hyperlipidemia from hypothyroidism, hyperadrenocorticism, diabetes mellitus, and familial hypertriglyceridemia.

Keratoconjunctivitis Sicca

Most cases are caused by lymphoplasmacytic dacryoadenitis.
Rarely seen with xerostomia (Sjögren-like syndrome)
Possible causes include drug therapy, atropine, sulfa drugs, etodolac, and anesthetic agents.
Others causes include canine distemper, FHV-1, and dysautonomia.

Uveal Tract, Lens, Fundus

Uveal Tract

Hyphema or Hemorrhage

Hypertension, rickettsial disease, trauma, coagulopathy, lymphoma, metastatic neoplasia

Protein or Fibrin Deposition

Trauma, feline infectious peritonitis (FIP), uveodermatologic syndrome, lens capsule rupture, rickettsial disease

Cellular (Hypopyon) or Granulomatous Infiltrates

Trauma, lymphoma, metastatic neoplasia, uveodermatologic syndrome, algae or yeast, lens capsule rupture, FIP, systemic mycoses, toxoplasmosis

Other infectious agents associated with uveal tract disease include feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), mycobacteria, FHV-1, *Bartonella* spp., *Ehrlichia* spp., *Leishmania donovani, Rickettsia rickettsii, Brucella canis, Leptospira* spp., and canine adenovirus.

Iris Abnormalities (Papillary Changes)

Anisocoria with FeLV
Miosis with Horner syndrome
Mydriasis with dysautonomia

Lens

Cataracts

Most common cause in dogs is hereditary.
Cataracts are frequent complication of diabetes mellitus.
Uveitis may also cause cataracts (most common cause in cats).
Other causes include hypocalcemia (hypoparathyroidism), electric shock, lightning strike, altered nutrition (e.g., puppies fed milk replacer).

Lens Luxation/Subluxation

Most often secondary to severe intraocular disease (uveitis)
May be primary in terriers

Fundus

Usually affected by diseases that extend from the uveal tract (*see* previous section) or from central nervous system (immune-mediated diseases such as granulomatous meningoencephalitis or neoplasia of CNS).

Papilledema

Optic nerve edema without hemorrhage, exudates, or blindness
Seen with increased intracranial pressure

Taurine Deficiency

Retinal degeneration
May also cause dilated cardiomyopathy

Retinal Visualization

Allows assessment of systemic condition including anemia (attenuated, pale vessels), hyperlipidemia (creamy orange hue to vessels), hyperviscosity (increased vessel tortuosity)

Systemic Hypertension

Causes extravasation of blood into retina, choroid, or subretinal space

Ocular Neoplasia

Orbital Neoplasia (presents as exophthalmos, strabismus, protrusion of the third eyelid, epiphora, and exposure keratitis)

- Osteosarcoma
- Multilobular osteosarcoma
- Fibrosarcoma
- Invasion of orbit by neoplasms of surrounding structures such as nose, sinuses, oral cavity, and orbital glands (nasal adenocarcinoma most commonly)
- Cats are more likely to have invasion of orbit from surrounding structures (fibrosarcoma, undifferentiated sarcoma, adenocarcinoma, lymphoma). Rarely see primary orbital neoplasia (squamous cell carcinoma, melanoma)

Adnexal Neoplasia (eyelid neoplasia common in dogs and rare in cats)

- 90% of eyelid tumors are benign (meibomian adenomas, melanomas, papillomas most commonly).
- Less common adnexal tumors include histiocytoma, malignant melanoma, adenocarcinoma, basal cell carcinoma, mast cell tumor, squamous cell carcinoma, hemangiosarcoma.
- Squamous cell carcinoma is the most common eyelid tumor in cats. Associated with sun exposure in cats that lack periocular pigmentation.

Surface Ocular Neoplasia (tumors of the conjunctiva, third eyelid, cornea)

- Dermoid
- Epibulbar or limbal melanocytoma
- Conjunctival neoplasia: hemangioma, hemangiosarcoma, mast cell tumor, lymphoma, squamous cell carcinoma, papilloma
- Third eyelid neoplasia: adenocarcinoma (most common), hemangiosarcoma, lobular adenoma, squamous cell carcinoma, melanoma

Intraocular Neoplasia (present with glaucoma, hyphema, corneal edema, buphthalmos, dyscoria, uveitis, retinal detachment, blindness)

- Anterior uveal melanoma (most common), 82% are benign in dogs, poorer prognosis in cats
- Other primary tumors of dogs include ciliary body adenocarcinoma and medulloepithelioma.
- Other primary tumors of cats include posttraumatic sarcoma and lymphoma.

Red Eye

Differential Diagnosis

Erythema of Primarily Conjunctival Vessels

- Corneal ulceration
- Eyelid abnormalities
- Dacryocystitis
- Cilia abnormalities
- Keratoconjunctivitis sicca
- Allergic conjunctivitis
- Bacterial or fungal keratitis
- Orbital disease

Erythema of Primarily Episcleral Vessels

- Anterior uveitis (low intraocular pressure)
- Glaucoma (high intraocular pressure)

Focal Erythema

Masses

- Prolapse of the gland of the third eyelid
- Neoplasia
- Episcleritis
- Nodular granulomatous episcleritis
- Granulation tissue

Hemorrhage

- Trauma
- Systemic disease (vasculitis, coagulopathy)

Retinal Detachment

Differential Diagnosis

Three Main Mechanisms—exudative, associated with retinal tears (rhegmatogenous), or traction pulling on retina

- Trauma—penetrating injuries such as animal bites, projectiles, or foreign bodies may result in retinal tears or induce intraocular hemorrhage, inflammation, or vitreous infection with subsequent traction retinal detachment. Typically unilateral, although strangulation can lead to bilateral retinal detachment
- Ocular anomalies such as severe retinal dysplasia, optic nerve colobomas, vitreous abnormalities, and retinal nonattachment (developmental failure of the two retinal layers to unite)
- Later-onset ocular anomalies such as cataracts and vitreous degeneration may lead to rhegmatogenous RD, especially

with rapid-forming or hypermature cataracts that lead to lens-induced uveitis.
- Hypertension is most often related to renal disease but may also be seen with hyperthyroidism and pheochromocytoma.
- Hyperviscosity—severe hyperlipidemia, hyperglobulinemia, polycythemia
- Neoplasia—most commonly due to multiple myeloma (hyperproteinemia and hyperviscosity) and lymphoma (infiltration of retina and choroid). Large intraocular tumors may induce traction retinal detachment.
- Chorioretinitis, retinochoroiditis
  - Bacteria (leptospirosis, brucellosis, bartonellosis
  - Rickettsia (ehrlichiosis, Rocky Mountain spotted fever)
  - Fungal (aspergillosis, blastomycosis, coccidioidomycosis, histoplasmosis, cryptococcosis)
  - Algae (geotrichosis, protothecosis)
  - Viral (canine distemper virus, FIP)
  - Secondary to retroviral infection (FeLV, FIV by predisposing to lymphosarcoma or an opportunistic infection like toxoplasmosis)
  - Parasitic (causes smaller areas of detachment—larval migrans of strongyles, ascarids, or *Baylisascaris* larvae. Toxoplasmosis, leishmaniasis, neospora, babesiosis.
- Immune-mediated disease—causes vasculitis with or without chorioretinitis
  - Systemic lupus erythematosus
  - Uveodermatologic syndrome
  - Granulomatous meningoencephalitis
- Toxic—trimethoprim/sulfa or ethylene glycol in dogs, griseofulvin in cats
- Idiopathic

Uveitis

Differential Diagnosis in the Dog(d) and Cat(c)

Systemic Infection

Bacterial

- Bacteremia or septicemia (d, c)
- Bartonellosis (d, c)
- Leptospirosis (d)
- Borreliosis (d)
- Brucellosis (d)

Rickettsial

- Ehrlichiosis (d, c)
- Rocky Mountain spotted fever (d)

Viral
- Canine adenovirus-1 (d)
- Feline leukemia virus (c)
- Feline immunodeficiency virus (c)
- Feline infectious peritonitis (c)

Mycotic
- Blastomycosis (d, c)
- Histoplasmosis (d, c)
- Coccidiomycosis (d, c)
- Cryptomycosis (d, c)
- Aspergillosis (d)

Algal
- Protothecosis

Parasitic
- Aberrant nematode larval migration
- *Toxocara* (ocular larval migrans) (d, c)
- *Dirofilaria* larvae (d)

Protozoan
- Toxoplasmosis (d, c)
- Leishmaniasis (d, c)

Immune-Mediated uveitis
- Idiopathic anterior uveitis (d, c)
- Lens-induced uveitis (d, c)
- Canine adenovirus vaccine reaction (d)
- Uveodermatologic syndrome (d) (primarily Akita and Arctic breeds)
- Pigmentary uveitis (d) (primarily Golden Retrievers)

Neoplasia
- Primary (d, c)
- Metastatic (most commonly lymphoma) (d, c)

Metabolic
- Diabetes mellitus (lens-induced uveitis) (d)
- Hyperlipidemia (d)

Trauma
- Blunt or sharp (d, c)

Miscellaneous Causes of Blood/Eye Barrier Disruption
- Hyperviscosity syndrome (d, c)
- Hypertension (d, c)
- Scleritis (d)
- Ulcerative keratitis (d, c)

SECTION XIII

Toxicology

Chemical Toxicoses

Toxicants

Kerosene, Gasoline, Mineral Seal Oil, Turpentine, Others
Pulmonary, central nervous system (CNS), and gastrointestinal (GI) signs: may lead to hepatotoxicity, renal toxicity, and cardiac arrhythmias

Naphthalene (Mothballs)
Vomiting, lethargy, seizures, acute Heinz body hemolytic anemia, methemoglobinemia, hemoglobinuria, renal failure

Ethanol, Methanol (Wood Alcohol)
CNS depression, behavioral changes, ataxia, hypothermia, respiratory and cardiac arrest

Ethylene Glycol
Early intoxication: ataxia, progresses to oliguric renal failure with renomegaly, vomiting, hypothermia, coma, and death

Soaps and Detergents
GI irritants

Household Corrosives
Toilet bowl cleansers, calcium/lime/rust removers, drain cleaners, oven cleaners, bleaches

Propylene Glycol
Ataxia, CNS depression

Phenol Products (Household Cleaners)
Cats particularly sensitive; hepatic and renal damage, ataxia, weakness, tremors, coma, seizures, respiratory alkalosis

Anticoagulant Rodenticides
Petechiae, ecchymosis, weakness, pallor, respiratory distress, CNS depression, hematemesis, epistaxis, melena, ataxia, paresis, seizures, sudden death

Zinc Phosphate
Anorexia, lethargy, weakness, abdominal pain, vomiting early after ingestion, progresses to recumbency, tremors, seizures, cardiopulmonary collapse, death

Cholecalciferol (Vitamin D) Rodenticides and Medications
Anorexia, CNS depression, vomiting, muscle weakness, constipation, bloody diarrhea, polyuria/polydipsia

Bromethalin Rodenticides
High-dose exposure: muscle tremors, hyperexcitability, vocalization, seizures, hyperesthesia, vomiting, dyspnea

Pyrethrin and Pyrethroid Insecticides
CNS depression, hypersalivation, muscle tremors, vomiting, ataxia, dyspnea, anorexia, hypothermia, hyperthermia, seizures, rarely death

Organophosphate and Carbamate Insecticides
Muscarinic signs (salivation, lacrimation, bronchial secretion, vomiting, diarrhea) and nicotinic signs (muscle tremors, respiratory paralysis), mixed signs (CNS depression, seizures, miosis, hyperactivity)

2,4-Dichlorophenoxyacetic Acid
Vomiting, diarrhea; greater exposure may cause CNS depression, ataxia, and hindlimb myotonia.

Lead (Paints, Batteries, Linoleum, Solder, Plumbing Supplies, Fishing Weights)
High-level exposure: vomiting, abdominal pain, anorexia, diarrhea, megaesophagus
CNS signs, behavioral changes, hysteria, ataxia, tremors, opisthotonos, blindness, seizures

Zinc
Acute ingestion: vomiting, CNS depression, lethargy, diarrhea
Chronic exposure: anorexia, vomiting, diarrhea, CNS depression, pica, hemolysis, regenerative anemia, spherocytosis, inflammatory leukogram, icterus, renal failure

Iron
Vomiting, diarrhea, abdominal pain, hematemesis, melena; rarely, progresses to multisystemic failure

Plant Toxicoses

Plants That Cause Hemolysis

Onion

Plants That Affect the Cardiovascular System

Cardiac glycoside toxicity: bradycardia with first-, second-, or third-degree atrioventricular (AV) block, ventricular arrhythmias, asystole, and sudden death; also see gastrointestinal (GI) signs
- Common oleander *(Nerium oleander)*
- Yellow oleander *(Thevetia peruviana)*
- Foxglove *(Digitalis purpurea)*
- Lily of the valley *(Convallaria majalis)*
- Kalanchoe *(Bryophyllum* spp.)

Azalea *(Rhododendron* spp.): weakness, hypotension, dyspnea, respiratory failure, GI signs

Yew (*Taxus* spp.): conduction disturbances, bradycardia, GI signs, weakness, seizures; poor prognosis once signs are seen

Plants Affecting the Gastrointestinal System

Oxalate-containing plants: gastric and ocular irritants
- Dumbcane (*Dieffenbachia* spp.)
- Philodendron (*Philodendron* spp.)
- Peace lily (*Spathiphyllum* spp.)
- Devil's ivy (*Epiprennum aureum*)
- Rhubarb leaves (*Rheum* spp.)

Philodendron may cause renal and central nervous system (CNS) signs in cats.

Chinaberry tree *(Melia azedarach):* vomiting, diarrhea, abdominal pain, hypersalivation, may progress to CNS signs and death

Cycad palms (*Cycas* spp.) or sago palms (*Macrozamia* spp.): vomiting, diarrhea, followed by lethargy, depression, liver failure, and death (dogs)

English ivy *(Hedera helix):* GI irritation, profuse salivation, abdominal pain, vomiting, diarrhea

Castor bean plant *(Ricinus communis):* ricin is among the most deadly poisons in the world; severe abdominal pain, vomiting, diarrhea, seizures, cerebral edema; prognosis for recovery is poor once clinical signs develop.

Holly (*Ilex* spp.), poinsettia *(Euphorbia pulcherrima),* mistletoe *(Phoradendron flavescens):* mild GI irritation, occasionally diarrhea, more serious effects with mistletoe

Amaryllis, jonquil, daffodil (family Amaryllidaceae), tulip (family Liliaceae), iris (family Iridaceae): ingestion of bulb associated with mild to moderate gastroenteritis

Autumn crocus *(Colchinum autumnale),* glory lily (*Gloriosa* spp.): colchicine, vomiting, diarrhea, abdominal pain, hypersalivation progressing to depression, multiple organ system collapse and death

Solanaceae family: tomato, eggplant, deadly or black nightshade, Jerusalem cherry-solanine, gastric irritant; may cause CNS depression and cardiac arrhythmias; nightshade can also contain belladonna.

Mushrooms: amanitine poisoning *(Amanita virosa, Amanita phalloides, Conocybe filaris),* orellanine poisoning *(Cortinarius orellanus, Cortinarius rainierensis),* monomethylhydrazine *(Gyromitra esculenta)*—severe hepatic disease; survivors of hepatic phase may succumb to renal tubular necrosis.

Plants Affecting the Neurologic System

Tobacco *(Nicotiana tabacum):* vomiting, CNS involvement, cardiac involvement

Hallucinogenic plants: psilocybins or "magic mushrooms," marijuana *(Cannabis sativa),* jimsonweed *(Datura stramonium),* thorn apple *(Datura metaliodyl),* blue morning glory *(Ipomoea violacea),* nutmeg *(Myristica fragrans),* peyote (family Cactaceae)

Nettle toxicity (family Urticaceae): hunting dogs, toxins contained in needles (histamine, acetylcholine, serotonin, formic acid), salivation, vomiting, pawing at mouth, tremors, dyspnea, slow and irregular heartbeat

Macadamia nuts: locomotor disturbances, tremors, ataxia, weakness

Yesterday, today, tomorrow (*Brunfelsia* spp.)

Plants Affecting the Renal System

Easter lily *(Lilium longiflorum)* and daylily (*Hemerocallis* spp.), possibly other lilies: toxic to cats, vomiting, depression, anorexia, leading to acute renal failure, poor prognosis without early treatment

Raisins/grapes: acute renal failure

Plants Causing Sudden Death

Seeds of many fruit trees (apple, apricot, cherry, peach, plum), contain cyanogenic glycosides

Venomous Bites and Stings

Snakes, Spiders, Others

Crotalids (Pit Vipers, Rattlesnakes, Copperheads, Water Moccasins)

Enzymatic and nonenzymatic proteins, local tissue damage: localized pain, salivation, weakness, fasciculations,

hypotension, alterations in respiratory pattern, regional lymphadenopathy, mucosal bleeding, obtundation, convulsions, anemia, echinocytosis, stress leukogram

Elapids (Coral Snakes)

Rare envenomation, signs delayed 10-18 hours, emesis, salivation, agitation, central depression, quadriplegia, hyporeflexia, intravascular hemolysis, respiratory paralysis

***Latrodectus* spp. (Widow Spiders)**

Hyperesthesia, muscle fasciculations, cramping, somatic abdominal pain (characteristic sign), respiratory compromise, hypertension, tachycardia, seizures, agitation, ataxia, cardiopulmonary collapse

Loxoscelidae (Recluse or Brown Spiders)

Cutaneous form: bull's-eye lesion, pale center with localized thrombosis, surrounded by erythema, develops into a hemorrhagic bulla with underlying eschar

Viscerocutaneous form: Coombs-negative hemolytic anemia, thrombocytopenia, disseminated intravascular coagulation (DIC)

Tick Paralysis

Dermacentor and *Haemaphysalis* ticks, ascending paralysis, lower motor neuron signs, megaesophagus and aspiration pneumonia in severe cases, spontaneous recovery a few days after tick removal

Hymenopteran Stings

Bites and stings of winged insects and fire ants

Toxic and allergic reactions (localized angioedema, urticaria, emesis, diarrhea, hematochezia, respiratory depression, death)

Helodermatidae Lizard (Gila Monster)

Salivation, lacrimation, emesis, tachypnea, respiratory distress, tachycardia, hypotension, shock

SECTION XIV

Urogenital Disorders

Differentiating between Urine Marking and Inappropriate Elimination in Cats

Urine Marking

- Generally vertical surfaces (can be horizontal)
- Marking behavior (may be territorial signaling or an anxiety- or conflict-induced response)
- Most common in intact males, females in estrous
- Adults
- Urine (rarely stool)
- Doors, windows, new objects, owner's possessions, frequently used furniture

Inappropriate Elimination

- Horizontal surfaces (rarely vertical)
- Elimination behavior
- Males or females, intact or neutered
- Any age
- Urine and/or stool
- Elimination in a variety of areas

Glomerular Disease

Types, Dogs and Cats

Glomerulonephritis
    Membranoproliferative form

- Type I (mesangiocapillary)
- Type II (dense deposit disease)

Proliferative glomerulonephritis (mesangial and endocapillary)
Crescentic type (rare)
Amyloidosis
Glomerulosclerosis
Focal segmental glomerulosclerosis
Hereditary nephritis
Immunoglobulin A (IgA) nephropathy
Lupus nephritis
Membranous glomerulopathy (most common in cats)
Minimal change glomerulopathy

Differential Diagnosis for Diseases Associated with Glomerular Disease, Dogs

Infection

Bacterial

Pyelonephritis
Pyoderma
Pyometra
Endocarditis
Bartonellosis
Brucellosis
Borreliosis
Other chronic bacterial infections

Parasitic

Dirofilariasis

Rickettsial

Ehrlichiosis

Fungal

Blastomycosis
Coccidioidomycosis

Protozoal

Babesiosis
Hepatozoonosis
Leishmaniasis
Trypanosomiasis

Viral

Canine adenovirus (type I) infection

Inflammation

Periodontal disease
Chronic dermatitis

Pancreatitis
Inflammatory bowel disease
Polyarthritis
Systemic lupus erythematosus (SLE)
Other immune-mediated diseases

Neoplasia
Lymphosarcoma
Mastocytosis
Leukemia
Systemic histiocytosis
Primary erythrocytosis
Other neoplasms

Miscellaneous
Corticosteroid excess
Trimethoprim-sulfa therapy
Hyperlipidemia
Chronic insulin infusion
Congenital C3 deficiency
Cyclic hematopoiesis in gray Collies

Familial
Amyloidosis (Beagle, English Foxhound)
Hereditary nephritis (Bull Terrier, English Cocker Spaniel, Dalmatian, Samoyed)
Glomerulosclerosis (Doberman Pinscher, Newfoundland)
Glomerular vasculopathy and necrosis (Greyhound)
Mesangiocapillary glomerulonephritis (Bernese Mountain Dog)
Atrophic glomerulopathy (Rottweiler)
Proliferative and sclerosing glomerulonephritis (Soft-Coated Wheaten Terrier)

Idiopathic

Differential Diagnosis for Diseases Associated with Glomerular Disease, Cats

Infection

Bacterial
Pyelonephritis
Chronic bacterial infections
Mycoplasmal polyarthritis

Viral
Feline immunodeficiency virus (FIV)
Feline infectious peritonitis (FIP)
Feline leukemia virus (FeLV)

Inflammation
- Pancreatitis
- Cholangiohepatitis
- Chronic progressive polyarthritis
- SLE
- Other immune-mediated diseases

Neoplasia
- Lymphosarcoma
- Leukemia
- Mastocytosis
- Other neoplasms

Miscellaneous
- Acromegaly
- Mercury toxicity

Familial

Idiopathic

Indications for Cystoscopy

- Localization of source of hematuria
- Urinary tract neoplasia
  - Determine extent and location of tumors
  - Obtain samples for cytology or histopathology
- Recurrent urinary tract infections
  - Examine for anatomic abnormalities or uroliths
  - Obtain samples for cytology, histopathology, or culture
- Urinary tract trauma
  - Examine for perforations, ruptures, and patency of urinary tract
- Urinary incontinence
  - Examine for ectopic ureters and/or urethral anomalies
  - Laser ablation of intramural ectopic ureters
  - Periurethral collagen injections for treatment of refractory urethral incompetence
- Urolithiasis
  - Confirm and remove small uroliths from bladder or urethra
  - Obtain uroliths for quantitative analysis and culture
  - Retrieve uroliths from bladder or urethra using stone forceps or stone basket
  - Fragment uroliths with laser lithotripsy
  - Fill bladder before and after voiding urohydropropulsion to remove small uroliths

Mammary Masses

Differential Diagnosis

- Benign mammary tumors
  - Mixed tumors (fibroadenomas)
  - Adenomas
  - Mesenchymal tumors
- Malignant mammary tumors
  - Solid carcinomas
  - Tubular adenocarcinomas
  - Papillary adenocarcinomas
  - Anaplastic carcinomas
  - Sarcomas (rare)
  - Most feline mammary tumors are adenocarcinomas
- Mammary hyperplasia
- Mastitis
- Granulomas
- Duct ectasia
- Skin tumors
- Lipomas
- Foreign bodies (e.g., BB pellets or shot may be confused with small mammary masses)

Prostatic Disease

Differential Diagnosis

Benign prostatic hyperplasia
Acute prostatitis
Chronic prostatitis
Abscess
Cyst
Prostatic neoplasia

- Adenocarcinoma most common
- Transitional cell carcinoma second most common
- Sarcomatoid carcinoma
- Primary and metastatic hemangiosarcoma
- Lymphoma

Diagnostic Evaluation

- History of lower urinary tract signs, penile discharge, hematuria, dysuria, tenesmus, obstipation, ribbon stools, stiff gait. Severe systemic signs suggest sepsis or systemic inflammation raises suspicion of acute prostatitis. Intact males are more predisposed to BPH and prostatitis.
- Digital rectal examination along with caudal abdominal palpation is a noninvasive initial screening test. The

rectum should be bilaterally symmetric, have a smooth and regular surface, have soft parenchyma, and not be painful to touch.

- Radiography of limited value for providing an actual diagnosis but may provide information about size, shape, contour, and location of the prostate. Prostatomegaly may cause dorsal displacement of the colon and cranial displacement of the urinary bladder. Mineralization with neoplasia, bacterial prostatitis, and abscessation may be apparent.
- Prostatic ultrasound is the most useful and practical imaging method. Normal prostate should have smooth borders and homogenous parenchymal pattern of moderate echogenicity. Ultrasound also offers the opportunity for guided aspirates and core biopsy sampling for culture, cytology, and histopathology.
- CT and MRI can evaluate size, shape, homogeneity of prostate and allow evaluation of intrapelvic lesions, metastatic spread, and ureteral obstruction.
- Definitive diagnosis requires cytologic, histologic, or bacteriologic evaluation of a prostate sample. Samples can be obtained using procedures such as semen collection, prostatic massage and wash, brush technique, fine needle aspiration, and biopsy.

Proteinuria in Dogs and Cats

Diagnostic Approach

- Stop use of nephrotoxic drugs.
- If proteinuria is insignificant (trace to 1+ dipstick reading and urine specific gravity > 1.035), there is no need for further workup.
- Perform urinalysis to exclude hemorrhage, infection, or inflammation as cause of proteinuria. If these conditions present, do urine culture. If these conditions are not present, do urine protein/creatinine ratio.
- Perform serum chemistry and CBC. Evaluate serum albumin and globulin.
  - Marked proteinuria ratio (UP/UC > 3) with quiet sediment and normal globulins or a polyclonal gammopathy is consistent with renal glomerular disease (glomerulonephritis, amyloidosis). Rule out causes of glomerulonephropathy such as heartworm disease, hepatozoonosis, immune-mediated diseases such as SLE, chronic infectious diseases such as borreliosis, feline leukemia virus, feline immunodeficiency virus, ehrlichiosis, other chronic inflammatory diseases, neoplasia, and hyperadrenocorticism).

- If no underlying disease found, may need renal biopsy to assess for glomerulonephritis or amyloidosis
- Proteinuria detected by precipitation testing but not dipstick or proteinuria associated with a monoclonal gammopathy may be caused by Bence Jones proteins. This requires a search for osteolytic or lymphoproliferative lesions. Ehrlichiosis may mimic myeloma. If Ehrlichia negative, protein electrophoresis in indicated. A monoclonal gammopathy suggests myeloma.

Pyelonephritis, Bacterial

Clinical Findings, Dogs and Cats

Fever
Renal pain
Leukocytosis
Anorexia
Lethargy
Cellular casts in urine sediment
Azotemia
Inability to concentrate urine
Polyuria/polydipsia
Ultrasonographic or excretory urographic abnormalities
- Renal pelvis dilatation
- Asymmetric filling of diverticula
- Dilated ureters

Bacteria in inflammatory lesions on histopathologic examination
Positive culture of ureteral urine collected by cystoscopy
Positive culture of urine obtained after rinsing bladder with sterile saline
Positive culture of urine obtained by ultrasound-guided pyelocentesis

Renal Disease

See **Glomerular Disease.**

Familial—Dogs And Cats

Amyloidosis—Beagle, English Foxhound, Shar-Pei, Abyssinian cat, Oriental shorthaired cat, Siamese cat
Renal Dysplasia—Lhasa Apso, Shih Tzu, Standard Poodle, Soft Coated Wheaten Terrier, Chow Chow, Alaskan Malamute, Miniature Schnauzer, Dutch Kooiker (Dutch decoy dog)
Fanconi syndrome (tubular dysfunction)—Basenji

Tubular dysfunction (renal glucosuria)—Norwegian Elkhound
Basement membrane disorder—Bull Terrier, Doberman Pinscher, English Cocker Spaniel, Samoyed
Membranoproliferative glomerulonephritis—Bernese Mountain Dog, Brittany Spaniel, Soft-Coated Wheaten Terrier
Primary glomerular disease—Rottweiler, Beagle, Pembroke Welsh Corgi, Newfoundland, Bullmastiff, Doberman Pinscher, Dalmatian, Bull Terrier, English Cocker Spaniel, Samoyed
Periglomerular fibrosis—Norwegian Elkhound
Polycystic kidney disease—Cairn Terrier, West Highland White Terrier, Bull Terrier, Persian cat
Multifocal cystadenocarcinoma—German Shepherd

Differential Diagnosis, Renal Tubular Disease

Cystinuria

Inherited proximal tubular defect
Many breeds of dogs including mixed breeds
Often leads to cystine calculi formation

Carnitinuria

Reported in dogs with cystinuria
May lead to carnitine deficiency and cardiomyopathy

Hyperuricosuria

Abnormal purine metabolism
- Dalmatian
- Dogs with primary hepatic disease

May lead to urate urolithiasis

Hyperxanthinuria (rare)

Seen in dogs receiving allopurinol to prevent urate uroliths
Congenital hyperxanthinuria seen in a family of Cavalier King Charles Spaniels

Renal Glucosuria

Primary renal glucouria (rare)
- Scottish Terrier, Basenji, Norwegian Elkhound, mixed breeds

Fanconi Syndrome

Inherited proximal tubular defect
Basenji most common
May lead to renal failure

Renal Tubular Acidosis

Rare tubular disorders that lead to hyperchloremic metabolic acidosis

- Proximal renal tubular acidosis
- Distal renal tubular acidosis

Nephrogenic Diabetes Insipidus

Any renal disorder that suppresses the kidneys' response to antidiuretic hormone (ADH)

Congenital (rare)

Acquired

- Toxic (*Escherichia coli* endotoxin)
- Drugs (glucocorticoids, chemotherapeutics)
- Metabolic disease (hypokalemia, hypercalcemia)
- Tubular injury or loss (polycystic renal disease, bacterial pyelonephritis)
- Medullary washout

Differentiating Acute from Chronic Renal Failure

Acute Renal Failure

- History of ischemia
- History of exposure to toxin
- Active urine sediment
- Good body condition
- Hyperkalemia (if oliguric)
- Normal to increased hematocrit
- Enlarged kidneys
- Potentially severe metabolic acidosis
- Severe clinical signs for level of dysfunction

Chronic Renal Failure

- History of previous renal disease
- History of polyuria/polydipsia
- Small irregular kidneys
- Nonregenerative anemia
- Normal to hypokalemia
- Normal to mild metabolic acidosis
- Inactive urine sediment
- Weight loss/cachexia
- Mild clinical signs for level of dysfunction

Renal Toxins in Dogs and Cats

Therapeutic Agents

Antibacterial Agents

Aminoglycosides

Sulfonamides

Nafcillin
Penicillins
Cephalosporins
Fluoroquinolones
Carbapenems
Rifampin
Tetracyclines
Vancomycin

Antifungal Agents
Amphotericin B

Antiviral Agents
Acyclovir
Foscarnet

Antiprotozoal Agents
Pentamidine
Sulfadiazine
Trimethoprim-sulfamethoxazole
Dapsone

Anthelmintics
Thiacetarsamide

Cancer Chemotherapeutics
Cisplatin/carboplatin
Methotrexate
Doxorubicin
Azathioprine

Immunosuppressive Drugs
Cyclosporine
Interleukin-2

Nonsteroidal Antiinflammatory Drugs (NSAIDs)

Angiotensin-Converting Enzyme (ACE) Inhibitors

Diuretics

Miscellaneous Agents
Dextran 40
Allopurinol
Cimetidine
Apomorphine
Deferoxamine
Streptokinase
Methoxyflurane
Penicillamine
Acetaminophen
Tricyclic antidepressants

Radiocontrast Agents

Nontherapeutic Agents

Heavy Metals

Lead
Mercury
Cadmium
Chromium

Organic Compounds

Ethylene glycol
Carbon tetrachloride
Chloroform
Pesticides
Herbicides
Solvents

Miscellaneous Agents

Mushrooms
Snake venom
Grapes/raisins
Bee venom
Lily

Pigments

Hemoglobin/myoglobin

Hypercalcemia

Causes of Acute Renal Failure in Dogs and Cats

Primary Renal Disease

Infection

Pyelonephritis
Leptospirosis
Infectious canine hepatitis

Immune-Mediated Disease

Acute glomerulonephritis
Systemic lupus erythematosus (SLE)
Renal transplant rejection

Renal Neoplasia

Lymphoma

Nephrotoxicity

Exogenous toxins
Endogenous toxins
Drugs

Renal Ischemia

Prerenal Azotemia

Dehydration/hypovolemia
Deep anesthesia
Sepsis
Shock/vasodilation
Decreased oncotic pressure
Hyperthermia
Hypothermia
Hemorrhage
Burns
Transfusion reaction

Renal Vascular Disease

Avulsion
Thrombosis
Stenosis

Systemic Diseases with Renal Manifestations

Infection
- Bacterial endocarditis
- Feline infectious peritonitis (FIP)
- Borreliosis
- Babesiosis
- Leishmaniasis

Pancreatitis
Diabetes mellitus
Hyperadrenocorticism
Hypoadrenocorticism
Hypocalcemia
Hypokalemia
Hypomagnesemia
Hyponatremia
Systemic inflammatory response syndrome (SIRS)
Sepsis
Multiple organ failure
Disseminated intravascular coagulation (DIC)
Heart failure
SLE
Hepatorenal syndrome
Malignant hypertension
Hyperviscosity syndrome
- Polycythemia
- Multiple myeloma

Urinary outflow obstruction
Envenomation

Causes of Chronic Renal Failure in Dogs and Cats

Inflammatory/infectious
- Pyelonephritis
- Leptospirosis
- Blastomycosis
- Leishmaniasis
- FIP

Familial/congenital (see p. 265)
Amyloidosis
Neoplasia
- Lymphosarcoma
- Renal cell carcinoma
- Nephroblastoma
- Tumor lysis syndrome
- Others

Nephrotoxicants (see p. 267)
Renal ischemia
Sequela of acute renal failure
Glomerulopathies (see p. 259)
Nephrolithiasis
Bilateral hydronephrosis
- Spay granulomas
- Transitional cell carcinoma at trigone obstructing both ureters
- Nephrolithiasis

Polycystic kidney disease
Urinary outflow obstruction
Idiopathic

Reproductive Disorders

Infertility—Differential Diagnosis, Canine Female

Normal Cycles

Improper breeding management
Failure to determine optimal breeding time
Female behavior
Infertile male
Elevated diestrual progesterone
- Early embryonic death
- Lesions in tubular system (vagina, uterus, uterine tubes)
- Placental lesions (brucellosis, herpes)

Normal diestrual progesterone
- Cystic follicles (ovulation failure)

Abnormal Cycles

Abnormal Estrus

Will Not Copulate
- Not in estrus
- Inexperience
- Partner preference
- Vaginal anomaly
- Hypothyroidism (possibly)

Prolonged Estrus
- Cystic follicles
- Ovarian neoplasia
- Exogenous estrogens
- Prolonged proestrus

Short Estrus
- Observation error
- Geriatric
- Ovulation failure
- Split estrus

Abnormal Interestrual Interval

Prolonged Interval
- Photoperiod (queen)
- Pseudopregnant/pregnant (queen)
- Normal breed variation
- Glucocorticoids (bitch)
- Old age
- Luteal cysts

Short Interval
- Normal (especially queen)
- Ovulation failure (especially queen)
- Corpus luteum failure
- "Split heat" (bitch)
- Exogenous drugs

Not Cycling
- Prepubertal
- Ovariohysterectomy
- Estrus suppressants
- Silent heat
- Unobserved heat
- Photoperiod (queen)
- Intersex (bitch)
- Ovarian dysgenesis
- Hypothyroidism (possibly)
- Glucocorticoid excess
- Hypothalamic-pituitary disorder
- Geriatric

Infertility—Differential Diagnosis, Canine Male

Inflammatory Ejaculate
- Prostatitis
- Orchitis
- Epididymitis

Azoospermia
- Sperm-rich fraction not collected
- Sperm not ejaculated
  - Incomplete ejaculation
  - Obstruction
  - Prostate swelling
- Sperm not produced
  - Endocrine
  - Testicular
  - Metabolic disorders

Abnormal Motility/Abnormal Morphology
- Iatrogenic
- Prepubertal
- Poor ejaculation
- Long abstinence

Abnormal Libido
- Female not in estrus
- Behavioral
- Pain
- Geriatric

Normal Libido
- Improper stud management
- Infertile female

Normal Libido/Abnormal Mating Ability
- Orthopedic
- Neurologic
- Prostatic disease
- Penile problem
- Prepuce problem

Penis, Prepuce, and Testes Disorders—Differential Diagnosis

Acquired Penile Disorders
- Penile trauma
  - Hematoma
  - Laceration
  - Fracture of os penis
- Priapism (abnormal, persistent erection)
- Neoplasia
- Vesicles

Warts
Ulcers

Congenital Penile Disorders
Persistent penile frenulum
Penile hypoplasia
Hypospadias (defect in closure of urethra)
Diphallia (duplication of penis)

Preputial Disorders
Balanoposthitis
- Bacteria infection
- Blastomycosis
- Canine herpesvirus

Phimosis
Paraphimosis

Testicular Disorders
Cryptorchidism
Orchitis/epididymitis
- *Mycoplasma* spp.
- *Brucella canis*
- *Blastomyces* spp.
- *Ehrlichia* spp.
- Rocky Mountain spotted fever
- Feline infectious peritonitis (FIP)

Testicular torsion
Testicular neoplasia
- Sertoli cell tumor
- Leydig cell tumor
- Seminoma

Drugs and Metabolic Disorders Affecting Male Reproduction

Glucocorticoids (hyperadrenocorticism, exogenous glucocorticoids)
  Decreased luteinizing hormone (LH), testosterone, sperm output, seminal volume, and libido; increased sperm abnormalities
Estrogens, androgens, anabolic steroids
  Decreased LH, testosterone, and spermatogenesis
Cimetidine
  Decreased testosterone, libido, and sperm count
Spironolactone, anticholinergics, propranolol, digoxin, verapamil, thiazide diuretics, chlorpromazine, barbiturates, diazepam, phenytoin, primidone
  Decreased testosterone and libido
Progestagens, ketoconazole
  Decreased testosterone

Amphoterin B, many anticancer drugs
Decreased spermatogenesis
Diabetes mellitus
Decreased libido and sperm count, abnormal semen
Renal failure, stress
Decreased libido and sperm count

Ureteral Diseases

Differential Diagnosis

Vesicoureteral Reflux

Primary: 7-12 weeks old—intrinsic maldevelopment of ureterovesical junction, self-limiting
Secondary to lower urinary tract obstruction, urinary tract infection, surgical damage, neurologic disease of bladder, ectopic ureters

Congenital Anomalies

Ectopic ureters
Ureterocele
Ureter agenesis
Ureter duplication

Acquired Ureteral Disease

Ureteral trauma
- Blunt trauma
- Penetrating trauma
- Iatrogenic damage during surgery

Inadvertent ligation and transection during ovariohysterectomy
Urinoma (paraureteral pseudocyst)
Ureteral obstruction
- Intraluminal (blood clot, calculus)
- Intramural (fibrosis, stricture, neoplasia)
- Extramural (retroperitoneal mass, bladder neoplasia, inadvertent ligature)

Calculi (nephroliths or nephrolith fragments that have migrated into the ureter)
- Calcium oxalate (most common in cat)
- Struvite (both struvite and calcium oxalate are most common in dog)

Neoplasia
- Transitional cell carcinoma
- Leiomyoma
- Leiomyosarcoma
- Sarcoma
- Mast cell tumor

- Fibroepithelial polyp
- Benign papilloma
- Metastatic neoplasia

Urinary Tract Infection (UTI)

Clinical Findings

Lower UTI

Dysuria
Pollakiuria
Urge incontinence
Gross hematuria at end of micturition
Cloudy urine
Foul odor to urine
Small, painful, thickened bladder
Palpable urocystoliths
Pyuria
Hematuria
Proteinuria
Bacteruria
Normal CBC

Upper UTI

Polyuria/polydipsia
Signs of systemic illness or infection
Possible renal failure
Fever
Abdominal pain
Kidneys normal to enlarged
Leukocytosis
Pyuria
Hematuria
Proteinuria
Bacteruria
Cellular or granular casts
Decreased urine specific gravity

Acute Prostatitis or Prostatic Abscess

Urethral discharge independent of micturition
Signs of systemic illness/infection
Fever
Painful prostate or abdomen
Prostatomegaly/asymmetry
Leukocytosis (±)
Pyuria
Hematuria

Proteinuria
Bacteruria
Inflammatory prostatic cytology

Chronic Prostatitis
Recurrent UTIs
Urethral discharge independent of urination
Possible dysuria
Normal complete blood count (CBC)
Pyuria
Hematuria
Proteinuria
Bacteruria
Prostatomegaly/asymmetry

Canine Lower Urinary Tract Disease—Differential Diagnosis

Urocystoliths
Struvite (magnesium ammonium phosphate)
Calcium oxalate
Purine (urate/xanthine)
Cystine
Calcium phosphate
Silica
Compound uroliths

Urethral Obstruction
Urethroliths (*see* Urocystoliths)
Blood clots
Urethral stricture
Neoplasia
- Transitional cell carcinoma
- Prostatic adenocarcinoma
- Leiomyoma
- Leiomyosarcoma
- Prostatic adenocarcinoma
- Squamous cell carcinoma
- Myxosarcoma
- Lymphoma
- Mast cell tumor

Proliferative urethritis
Urinary bladder entrapment in perineal hernia
Trauma
- Penile fracture

Urinary Tract Trauma
Contusion (bladder or urethra)
Urethral tears

Rupture of bladder (blunt trauma, secondary to pelvic fracture, penetrating wound)
Avulsion of bladder or urethra
Penile fracture

Inflammation (Bladder or Urethra)
Bacterial UTI
Fungal UTI
Polypoid cystitis
Emphysematous cystitis
Cyclophosphamide-induced cystitis
Parasitic cystitis *(Capillaria plica)*

Feline Lower Urinary Tract Disease—Differential Diagnosis

Feline idiopathic cystitis
Urethral plug (obstructive feline idiopathic cystitis)
Urolithiasis
- Struvite
- Calcium oxalate
- Urate
- Cystine

Bacterial cystitis (less common in cats than in dogs)
Stricture
Neoplasia

Uroliths, Canine

Characteristics

Calcium Oxalate Monohydrate or Dihydrate
Radiopaque
Acidic to neutral pH
Sharp projections or smooth uroliths; calcium oxalate dihydrate uroliths may be jackstone shaped
Not associated with urinary tract infection
Calcium oxalate dihydrate crystals: square envelope shape
Calcium oxalate monohydrate crystals: dumbbell shaped

Struvite (Magnesium-Ammonium-Phosphate)
Radiopaque
Alkaline pH
Smooth to speculated if single; smooth and pyramidal in shape if multiple
Associated with infection with urease-producing bacteria (*Staphylococcus, Proteus, Ureaplasma* spp., *Klebsiella, Corynebacterium*)
"Coffin lid"–shaped crystals

Urate/Xanthine
Radiolucent to faintly radiopaque
Acidic pH
Smooth uroliths
Not associated with infection
Yellow-brown "thorn apple" (spherical) or amorphous crystals

Cystine
Faintly to moderately radiopaque
Acidic pH
Smooth, round uroliths; staghorn-shaped uroliths if nephroliths present
Not associated with infection
Hexagonal-shaped crystals

Calcium Phosphate
Radiopaque
Alkaline to normal pH for hydroxyapatite, acidic for brushite
Small, variably shaped uroliths for hydroxyapatite
Smooth, round or pyramidal for brushite
Not associated with infection
Amorphous phosphate crystals or thin prisms (calcium phosphate)

Silica
Radiopaque
Acidic to neutral pH
Jackstone-shaped uroliths
Not associated with infection
No crystals

Vaginal Discharge

Differential Diagnosis

Cornified Epithelial Cells
Normal proestrus
Normal estrus
Contamination of skin or epithelium
Ovarian remnant syndrome
Abnormal source of estrogen
- Exogenous
- Ovarian follicular cyst
- Ovarian neoplasia

Contamination of squamous epithelium

Mucus
- Normal late diestrus or late pregnancy
- Normal lochia
- Mucometra
- Androgenic stimulation

Neutrophils

Nonseptic (no microorganisms seen)
- Vaginitis
- Normal first day of diestrus
- Metritis or pyometra

Septic
- Vaginitis
- Metritis
- Pyometra
- Abortion

Peripheral Blood
- Subinvolution of placental sites
- Uterine or vaginal neoplasia
- Trauma to reproductive tract
- Uterine torsion
- Coagulopathies

Cellular Debris
- Normal lochia
- Abortion

Pain Diagnosis

Acute Pain Assessment

Subjective evaluation of pain in animals relies on observation and interpretation of animal behavior. Pain may be indicated by loss of normal behaviors or appearance of abnormal behaviors.

Dogs

- Restless, agitated, delirious
- Lethargic, withdrawn, dull, obtunded
- May ignore environmental stimuli
- Abnormal sleep-wake cycle, inability to sleep
- May bite, lick, or chew painful area
- Adopt abnormal body positions to cope with pain
- Ears held back, eyes wide open with dilated pupils or closed with a dull appearance
- Disuse or guarding of painful area
- Vocalization (whimper, yelp, whine, groan, yowl)
- May become more aggressive and resist handling or palpation or may become more timid and seek increased contact with caregivers

Cats

- Hide, stay to back of cage
- Behavior may be mistaken for fear or anxiety
- May sit very quietly and pain may be missed by those looking for more active signs of pain
- May continue to purr while in pain
- May growl with ears flattened
- May attempt escape
- Lack of grooming
- Hunched posture, statue-like appearance
- Reduced or absent appetite
- Tail flicking

Acute Pain Preemptive Scoring System (examples in each category)

Minor Procedures: No Pain

- Physical examination, restraint
- Radiography
- Suture removal, cast application, bandage change
- Grooming
- Nail trim

Minor Surgeries: Minor Pain

- Suturing, debridement
- Urinary catheterization
- Dental cleaning
- Ear examination and cleaning
- Abscess lancing
- Removing cutaneous foreign bodies

Moderate Surgeries: Moderate Pain

- Ovariohysterectomy, castration, caesarean section
- Feline onychectomy
- Cystotomy
- Anal sacculectomy
- Dental extraction
- Cutaneous mass removal
- Severe laceration repair

Major Surgeries: Severe Pain

- Fracture repair, cruciate ligament repair
- Thoracotomy, laminectomy, exploratory laparotomy
- Limb amputation
- Ear canal ablation

Chronic Pain Assessment

- Clinical signs of chronic pain depend on underlying cause and pathologic state.
- Range from subtle to obvious
- May see acute flareups that require changes in treatment (e.g., osteoarthritic dog that experiences acute pain after excessive strenuous activity
- Decreased activity
- Reluctance to rise or play
- Changes in sleep patterns
- Changes in appetite
- Changes in social interaction and grooming habits
- Withdrawal, aggression
- Owner observations are extremely important